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OBSERVATIONS ON 1,078 PERINATAL DEATHS

BY

A. M. STEWART, J. W. WEBB*, AND D. HEWITT

From the Social Medicine Unit, Oxford University

A cause of death is the morbid condition or other disease process, abnormality, or injury leading directly or indirectly to death . . . From the standpoint of the prevention of deaths it is important to cut the chain of events or institute the cure at some point. The most effective public health objective, of course, is to prevent the precipitating cause from operating. For this purpose the most useful single statistic is that relating to the underlying cause of death which may be defined as (*a*) the disease or injury which initiated the train of morbid events leading directly to death, or (*b*) the circumstances of the accident or violence which produced the fatal injury . . . Symptoms or modes of dying such as heart failure, asthenia etc., are not considered to be causes of death for statistical purposes. (W.H.O., 1948).

In the vast majority of cases these elementary rules of procedure present little difficulty to the doctor who has to sign a death certificate. Mistakes are sometimes made, but each certificate is carefully scrutinized at the General Register Office and if there is any reason to suppose that the stated cause of death merely describes the mode of dying it is promptly returned for amendment. In the case of stillbirths and neonatal deaths, however, the rules cannot be strictly enforced. The absence of definite signs of disease (or the co-existence of several equally lethal conditions), combined with the difficulty of following intra-uterine events, frequently makes it impossible to express a reasoned opinion as to the cause of death. It is obvious, for example, that prematurity cannot possibly have "initiated the train of events leading directly to death". Nevertheless every year thousands of certificates giving this as the cause of death are accepted by the General Register Office, and "prematurity" regularly takes its place as a cause of death both in official vital statistics and in the international list of diseases.

At first sight certificates which name something more precise, like a congenital defect, as the cause of death seem more informative than those which attribute death to prematurity. But a moment's thought will show that it is the *secondary* nature of prematurity and not any vagueness in the term (or any doubt whether a baby should be so described) that makes it so unrevealing as a cause of death. Since maldevelopment, like under-development, is the end-result of an unknown process, even certificates with such precise diagnostic terms as anencephalus and exomphalos do no more than describe a mode of dying.

The realization that a medical classification of stillbirths and neonatal deaths is unsatisfactory has led workers to stress the importance of non-medical conditions, and to study social and genetic factors which (though they will never gain admission to the International list) are nevertheless on a par with some categories now accepted as causes of death (Baird and Illsley, 1953; Douglas, 1950; Karn and Penrose, 1952; Sutherland, 1949; Woolf, 1947). The results of such investigations may eventually provide us with a more satisfactory nomenclature. Meanwhile there is so much confusion about what are proximate and remote causes of death in infancy, and what are merely modes of dying, that it may be of value to take a group of live and dead babies and, *without prejudice to the question of causation*, compare the frequency of various observations made before, during, and immediately after delivery. With this end in view we have examined the antenatal and obstetrical records of just over a thousand stillbirths and neonatal deaths, and have compared them with the records of an equal number of babies who survived beyond the age of 4 weeks.

Material and Methods

The records form part of a survey in which five Public Health departments participated. Each centre agreed that data should be collected for two categories:

(1) All stillbirths and neonatal deaths occurring in a given year (1952–3).

(2) All other babies born (to mothers normally resident in the area) on certain stated days of each month.

* In receipt of a grant from the Medical Research Council.

Existing records of antenatal, obstetrical, and postnatal supervision were assembled, and Health Visitors were asked to collect certain additional facts when they paid their first postnatal visit to the house. All the records were transcribed onto printed cards and in each area one or two medically qualified persons were responsible for the correct interpretation of the clinical data. The observations were not restricted to any special group of babies; domiciliary and institutional deliveries, multiple and single births, and cases with and without antenatal or obstetrical supervision were included in the survey.

Some regions sent the records of a disproportionately large number of surviving babies, but, to prevent regional factors from affecting the calculations, the present study has used an equal number of live and dead babies from each region.* The cases were distributed as follows:

	Live	*Dead*
Northumberland	450	450
Northamptonshire	292	292
Coventry	122	122
Salford	115	115
West Riding of Yorkshire (six divisions)	99	99

Total number: 1,078 stillbirths and neonatal deaths (Dead Sample) and 1,078 babies who survived to 4 weeks (Live Sample).

Neither sample includes any multiple births but the Dead Sample includes all other available cases.

Age and Parity Effects

Table I shows a preliminary analysis of the material in terms of maternal age and parity. The cells of the Table show:

(1) Total number of live and dead babies whose mothers fell into the stated age and parity group.

(2) Ratio of the number of dead babies to the number of live babies.

(3) Statistical significance of any departure of this ratio from unity.†

The Table illustrates two well-established features of perinatal mortality, namely, the above-average risk of death for first babies, and for all infants born to older mothers, particularly first babies.

In the present sample the most favourable condition for survival was enjoyed by the second and third children of a mother who was still under 26 years of age.

Among the propositions which may be based on the figures in Table I is the following:

If babies born to mothers over 33 years of age had suffered no greater risk of death than those born to younger mothers, then about 100 deaths, or 9 per cent. of the total would not have occurred.

* An analysis of the stated causes of death revealed no significant differences between the five regions.

† This was assessed by means of a χ^2 comparison of actual and "expected" numbers of live and dead babies, after standardizing for age in the case of parity, and for parity in the case of age.

TABLE I

COMPARATIVE DISTRIBUTION BY MOTHER'S AGE AND PARITY OF 1,078 LIVING AND 1,078 DEAD OR STILLBORN INFANTS, SHOWING RATIO OF NUMBER DEAD TO NUMBER LIVING IN EACH GROUP

Age (yrs.)	Parity			
	First	Second or Third	Fourth or Later	All Parities
25 or Under ..	479 1·10	274 0·71**	27 1·45	780 0·95
26 to 32 ..	233 1·14	458 0·75**	177 0·88	868 0·87
33 or Over ..	68 2·40**	233 1·03	207 1·59**	508 1·36***
All Ages	780 1·18**	965 0·80***	411 1·22	2,156 1·00

Significance levels:
5 per cent. *
1 per cent. **
0·1 per cent. ***

It is of interest to consider the logical parallel between this and another proposition which can be supported by the survey findings:

If babies with congenital defects had suffered no greater risk of death than other babies, then about 257 deaths or 24 per cent. of the total number would not have occurred.

No one would take the first proposition to mean that 9 per cent. of the deaths had been *caused* by the fact that the mother was over the age of 33. But current usage would allow the latter proposition to be translated into "24 per cent. of deaths were caused by congenital defects". In neither case can a statement about cause of death be deduced from the original proposition, though it is worth noting that aging of the mother might properly be regarded as an "underlying cause", whereas a congenital defect merely describes a "mode of dying". We suggest therefore that the distinction is based purely on the observation that the case fatality associated with congenital defect is much higher than that associated with excessive age in the mother. That is to say, the basis for the selection of "the cause of death" in a large number of stillbirths and neonatal death certificates is, implicity, no more than a statistical association between certain abnormal findings and the subsequent birth of a dead or moribund infant.

Such being the case, it is clearly important to estimate as precisely as possible the case fatality associated with a number of antecedent events. Tables II–V show the relative frequency of 25 items in the records of the dead and living babies, the total number of times each item was recorded, and an indication whether or not the relative frequency differs significantly from unity.

The significance tests were based on figures which had been standardized in the same age-parity groups of Table I, but the relative frequencies are deliberately based on "crude" or unstandardized figures, adjusted only for numbers "not stated" in each sample. For two reasons the relative frequencies do not provide an unbiased estimate of the risk of death among affected and unaffected babies. In the first place they take no account of the small number of cases in which manoeuvres such as craniotomy were carried out *after* the death of the foetus. Secondly, an unbiased estimate of risk would have to take account of the ratio of dead to living infants in the population from which the samples were drawn,* a ratio which has not been considered here.

Risks associated with certain Abnormal Events

From the nature of the investigation it was unlikely that any "new" observations would be made. The interest of the following Tables lies, therefore, not in the selection of items which appear as bad risks, but in the attempt to express certain observed facts as measured quantities. The items for which risks have been calculated have been divided into four groups.

The first (Table II) includes a number of signs and symptoms (noted before, during, and after delivery) which are generally recognized as abnormal or likely to lead to difficulties.

The second group (Table III) comprises certain active steps taken by the doctors in charge, presumably because their cases presented unusual or potentially dangerous features.

Table II

COMPARISON OF 1,078 STILLBIRTHS AND NEONATAL DEATHS WITH 1,078 BABIES WHO SURVIVED TO ONE YEAR

Risk of foetal death associated with certain signs and symptoms

Signs and Symptoms	Number of Cases	Ratio†	Significance‡
Extreme Prematurity[1]	297	98·1	***
Hydramnios	47	46·1	***
Prolapsed Cord	31	30·0	***
Antepartum Haemorrhage (excluding placenta praevia)	131	13·7	***
Congenital Defects	283	9·9	***
Abnormal Presentation (multiparae)	109	5·4	***
Placenta Praevia	30	5·0	**
Moderate and Severe Toxaemia[4]	204	5·0	***
Moderate Prematurity[2]	199	4·7	***
Antenatal Injury or Operation	47	3·0	**
Threatened Abortion[5]	96	2·6	***
"Dry" Labour	16	2·4	
Precipitate and Unattended Labour	82	1·9	**
Abnormal Presentation (primiparae)	79	1·9	**
Anaemia (antenatal)[6]	170	1·7	***
Postmature[3]	90	1·4	
Other Illness (antenatal)	224	1·2	
Slight Toxaemia	129	1·1	
Virus Infection (antenatal)	32	1·0	

[1] Under 4 lb. birthweight or born more than 60 days before date of expected delivery.
[2] Over 4 and under 5½ lb. birthweight or born 41–59 days before date of expected delivery.
[3] Over 10 lb. birthweight or born over 30 days after date of expected delivery.
[4] Requiring rest in bed.
[5] Bleeding *per vaginam* any time during antenatal period.
[6] Haemoglobin = 75 per cent. or less, or mother described as "anaemic".
† *i.e.* Ratio of the times recorded in the Dead Sample to the times recorded in the Live Sample.
‡ *** = $P<0{\cdot}001$ ** = $P<0{\cdot}01$ * = $P<0{\cdot}05$

* Let A = the proportion of affected among the living infants,
B = the proportion of affected among the dead infants,
D = the proportion of dead infants in the population. Also let
$K = A + D(B - A)$. Then an unbiased estimate of relative risk would be given by $B(1 - K)/K(1 - B)$. For example, assuming a perinatal mortality rate of 40 per thousand, the relative risk for the "moderately premature" infants may be estimated as 4·47, compared with the relative frequency (B/A) in Table II of 4·69.

Table III

COMPARISON OF 1,078 STILLBIRTHS AND NEONATAL DEATHS WITH 1,078 BABIES WHO SURVIVED TO ONE YEAR

RISK OF FOETAL DEATH ASSOCIATED WITH CERTAIN TYPES OF ACTIVE INTERVENTION

Intervention	Number of Cases	Ratio	Significance
Craniotomy	14	∞	***
Internal Manipulation	28	6·1	***
Forceps (multiparae)	33	5·7	***
Caesarean Section	68	2·6	**
External Version	63	1·5	
Forceps (primiparae)	90	1·1	

The third group (Table IV) is more mixed. Two of the items (habitual abortion and Rhesus factor) are recognized as "causes" of stillbirth, and one (illegitimacy) frequently features in official vital statistics. The fourth item (pre-marital conception) is included because it probably has something in common with illegitimacy.

Table IV

RISK OF FOETAL DEATH ASSOCIATED WITH CERTAIN SOCIAL AND CONSTITUTIONAL BACKGROUNDS

Background	Number of Cases	Ratio	Significance
Habitual Abortion[1]	55	3·2	***
Premarital Conception (legitimate)	94	1·8	*
Premarital Birth (illegitimate)	89	1·4	
Rhesus-Negative (multiparae)	198	1·0	

[1] Ratio of miscarriages and stillbirths to live birth greater than unity (*i.e.* more unsuccessful than successful pregnancies).

Table V (overleaf) describes risks associated with different types of maternal physique. It differs from the preceding Tables in that all the mothers belonged to one of the nine body-build groups so that there were bound to be some groups in which the ratio of deaths to survivors was less than unity, and in that none of the nine sub-groups are abnormal, in the usually accepted sense.

TABLE V

RISK OF FOETAL DEATH ASSOCIATED WITH DIFFERENT TYPES OF MATERNAL PHYSIQUE†

Build	Height	Number of Cases	Ratio		Significance
Obese	short	39	2·1**	1·6	***
	average ..	146	1·5*		
	tall	27	1·5		
Average	short	179	1·1	1·0	
	average ..	1,005	1·0		
	tall	207	0·7		
Thin	short	105	1·2	1·0	
	average ..	180	1·0		
	tall	65	0·8		

† Description given by Health Visitors 3–4 weeks after delivery.

The grave prognosis attached to such abnormal signs as hydramnios, prolapsed cord, antepartum bleeding, and congenital defects is clearly demonstrated in Table II, as is also the very different type of risk associated with severe and mild grades of prematurity and toxaemia. In the live sample abnormal presentations (other than cord) were nearly three times as common among primiparae as among multiparae, but for the latter group the risk of foetal death was much greater and (in the present series) actually exceeded the risk associated with placenta praevia. Abnormal presentations in first births were nearly twice as hazardous as normal presentations and about as dangerous as having a precipitate delivery without supervision.

One of the most disappointing features of the survey was the number of cases returned with no haemoglobin records. A large majority of the mothers had had at least one blood test—as witnessed by the large numbers of Kahn tests, Rhesus factors, and ABO blood groups—but only in one region was a haemoglobin value automatically recorded. Nevertheless, it is clear that anaemia in the mother has unfortunate repercussions on the baby, for in the group of 170 cases where either the haemoglobin was (on one occasion only) less than 76 per cent. or the mother was said to be "anaemic" there was an excess of infant deaths of nearly 70 per cent.

The survey also showed that routine antenatal records cannot be relied upon as sources of morbidity data in the antenatal period. Routine testing of the urine and blood was done at all the clinics, but there was no guarantee that minor diseases (other than slight toxaemia of pregnancy) were consistently recorded. The whole sample yielded 47 examples of major injury or operation, 32 cases of virus infection (including influenza), and 224 other illnesses. In the accident and operation group the number of deaths recorded was nearly three times greater than the "expected" number, but for the virus infections and other illnesses there was no appreciable increase in general risk. The number of cases in which there was premature loss of the amniotic fluid (16) was too few to obtain a significant result, but in this small group the proportion of deaths and survivors was roughly the same as for the 96 cases in which bleeding *per vaginam* was recorded some time during the antenatal period.

Five types of active intervention are analysed in Table III. One of these (craniotomy) is, by definition, universally fatal, and one (forceps) has been separately studied in primiparae and multiparae. No special risk attached to the use of forceps in first births but when applied to later births the infant frequently died either during or shortly after delivery. Approximately half of the Caesarean sections were begun before and half after the onset of labour. This proportion applied to both primiparae and multiparae, and in both cases the operation was performed more than two and a half times as frequently in the dead as in the living sample. External version had been attempted in 63 cases and for this group the risk of foetal death was 45 per cent. above standard.

A question which is frequently asked is "What are the chances against a woman, who is pregnant and has had several miscarriages or stillbirths, producing a live baby?". In the present sample, where habitual abortion was defined as "more unsuccessful than successful pregnancies" (and therefore included primiparae who had had one miscarriage), there was three times the normal chance that the baby would be dead within a month of delivery. This is about the same as the overall risk for abnormal presentations (all parities combined). Several deaths were ascribed to haemolytic disease, but these did not bring about a general excess of deaths among Rhesus-negative multiparae.

In England and Wales, the stillbirth and neonatal death rates among illegitimate babies, though still excessive, have been falling faster than the national rates. In the present sample the survival rate for illegitimate infants was slightly below par, but the difference between the observed and expected number of deaths was not statistically significant. There were, however, at least 94 mothers who married after their babies were conceived but before they were born, and in this group the number of stillbirths and neonatal deaths was significantly greater than the expected number.

Baird and Illsley (1952) have reported an inverse association between height of mother and foetal death rate. The classification of height in Table V is based, not on precise measurements, but on the Health Visitor's description of the mother as "tall", "medium", or "short". Nevertheless these three groups were found to differ significantly, with tall mothers again showing to advantage. Health Visitors were also asked to characterize the build of each woman as "obese", "medium"', or "thin" "Medium" and "thin" women did not differ in their ability to produce live infants, but among the 212 women described as "obese" the risk of stillbirth or neonatal death was 60 per cent. above the standard. This risk appeared to be still greater among the women who were described as both "obese" and short".

Virus Infections in the Antenatal Period

A topic which has stimulated much interest in recent years is the possibility of an association between virus infection during pregnancy and the subsequent birth of a malformed infant. It has been suggested that some of the earlier investigations of this topic are inadequate because the medical history (having been collected retrospectively) may have been biased by the known outcome of the pregnancy (Logan, 1951). The present investigation is not open to this criticism, for the records of antenatal illnesses, though admittedly incomplete, were compiled *before* delivery. In the live sample the congenital malformations were mainly of a trivial and uninteresting nature*. There were, however, in the dead sample sixteen cases in which the mother was known to have had a virus infection. In this small group there were seven babies with congenital malformations and nine without. According to the overall frequency of congenital malformations in the dead sample as a whole, the "expected" numbers were 3·8 and 12·2 respectively. These numbers are too small for the ordinary χ^2 treatment, but an exact one-tailed test based on the expansion of $(0{\cdot}238 + 0{\cdot}762)^{16}$ shows that the observed and "expected" numbers do in fact differ at the 5 per cent. level of significance.

* One mother who had influenza in the second month of pregnancy produced a baby with congenital heart disease. As the baby survived to 10 weeks it is not included in the following analysis.

The sixteen virus infections in the dead sample included eleven cases of influenza, four of rubella, and one of infective hepatitis. Three cases were undated, six occurred in the first 3 weeks of pregnancy, and seven in the later months.

Summary

Certificates of stillbirth and neonatal death frequently contain terms which may be said to described the "mode of dying" rather than the "cause of death". This is inevitable while all but a handful of the true causes remain unknown. The justification for the terms in current use is a statistical one (*i.e.* a high case fatality associated with certain events noted before, during, or shortly after delivery). In an attempt to make this situation more explicit a comparison has been made of the frequency of some of these events in the records of 1,078 dead babies and of an equal number of babies who survived to the age of 4 weeks. None of the findings which emerged are altogether new, but it is hoped that the form of the analysis may set familiar facts in a fresh perspective and so help to stimulate a more radical approach to the medical problems of perinatal mortality.

It is unfortunately not possible to mention by name all the people who took part in the survey, but we hope they will identify themselves with Dr. Tilley (*Northumberland*), Dr. C. M. Smith (*Northamptonshire*), Dr. Clayton (*Coventry*), Dr. Sproul (*Salford*), and Dr. Wood-Wilson (*West Riding of Yorkshire*), who organized the field work and to whom we offer our most grateful thanks.

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MUSTARD GAS POISONING, CHRONIC BRONCHITIS, AND LUNG CANCER

AN INVESTIGATION INTO THE POSSIBILITY THAT POISONING BY MUSTARD GAS IN THE 1914–18 WAR MIGHT BE A FACTOR IN THE PRODUCTION OF NEOPLASIA

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Introduction

Mustard gas ($\beta\beta$-dichlor-ethyl-sulphide) and its analogues, the nitrogen mustards, are known to be carcinogenic to experimental animals (Boyland and Horning, 1949, Heston, 1953a, b). It was first used on the Western Front in the 1914–18 war on the night of July 12–13, 1917, and after that date was used so extensively that areas of the country became saturated with it and had to be abandoned by both sides. Because of this persistence it is not possible to assume that any man serving in the front line after July 12, 1917, escaped some exposure to the gas.

Between this date and the end of the war the total number of British cases treated for war gas poisoning is recorded as 160,970, and 80 per cent. of these are estimated to be due to mustard gas (Medical Services Diseases of the War, 1923). 124,702 of these cases were admitted to hospitals, and 4,167 died before discharge. These figures must be an underestimate of the total British casualties, since they do not include the unknown number of men who were gassed and taken prisoner.

An experience of this sort, where a chemical stimulus of an easily identifiable type is applied to a human population for a short time, at a known date, resembles in some ways a carefully planned animal experiment, and the size of the operation should provide ample material for an investigation into any possible carcinogenic action of the gas.

Methods and Materials

The ideal method of investigation would be to take all or a random sample of the men known to have been gassed and to follow up their histories until the present date. This could not be done since the absence of extensive and reliable morbidity data for neoplastic diseases compels the use of mortality data, and the Registrar-General's records cannot answer the questions "Is this person dead or not, and if so when and why?". Before a particular death certificate can be traced, it is necessary to know firstly that death has taken place, and secondly the approximate date and the district where the death was registered.

Fortunately, in the present circumstances, an alternative method was available, to follow up the histories of those men who were pensioned for the effects of mustard gas poisoning, since if death had occurred sufficient data would be recorded to enable the death certificates to be traced.

The Ministry of Pensions and National Insurance has complete records of all men who were receiving a pension in 1930, but this was the earliest date at which the records were complete. The disability for which the pension was granted, and often the grant of the pension itself, were of course in existence for varying periods before this date. On January 1, 1930, 1,267 men in England and Wales were receiving a pension for the effects of mustard gas poisoning resulting from the 1914–18 war. A small number of cases in Scotland and Ireland were excluded, since it would otherwise have been necessary to prepare extensive additional analytical tables for these countries. Apart from these cases, the whole of the available data is used, so that no question of further selection arises. The mortality experienced by these 1,267 men was examined from January 1, 1930, until December 31, 1952, this closing date being determined because it was the end of the last year for which the Registrar-General's Annual Reports had become available. This mortality experience (subsequently referred to as the experience "found") was compared with a standard ("expected") mortality experience based on the male population (including non-civilians) of England and Wales, calculated by a

method (see statistical appendix) that makes allowances for age-specific and secular changes of mortality rates.

Since data for environmental cancer studies on carefully and completely defined populations are scanty, arrangements are being made to ensure that adequate records of the men surviving after the end of 1952 are maintained. It will then be possible to make periodical surveys of the mortality experience, until eventually a complete mortality study from 1930 until the demise of all the men concerned can be made. Such a study might provide interesting information about any possible alteration in cancer mortality at more advanced ages, and help to elucidate whether the increase of lung cancer found in two of the series discussed below represents an absolute increase in the carcinogenic process or merely an earlier induction in susceptible subjects.

Discussions had indicated that there were two opinions about the type of possible carcinogenic effect of mustard gas. One suggested that the effect might be specifically confined to the respiratory tract, the other that the effect might be non-specific and affect the general process of neoplasia. Since the number of deaths from neoplastic disease in the series was too small to warrant a complete analysis by site, analytical tables were selected for the two disease classifications "all neoplasms" (including malignant tumours, non-malignant or undefined tumours, leukaemia and lymphadenoma) and "cancer of the lung and pleura". By subtraction, a third classification, "neoplasms other than cancer of the lung and pleura", is obtained.

The problem of the possible effect of mustard gas was studied by comparing the mortality expected and that found from "cancer of the lung and pleura" and from "neoplasms other than cancer of the lung and pleura". In addition to these, deaths from "all causes" were also studied.

As will be shown later, the men in the mustard gas series experienced an excessive mortality from bronchitis, and the case histories were examined to see why a pension was being issued in 1930. This investigation revealed that, although the *label* in each case was "mustard gas poisoning" or some similar phrase, the *reason* for granting the pension was not that the man had been gassed but that in 1930 there were sufficient clinical findings present to warrant the view that permanent damage had been sustained. In 81 per cent. of the cases the pension was given because of bronchitis, bronchiectasis, emphysema, or fibrosis of the lung, and in most of the remaining 19 per cent. there was clear evidence of bronchitis. Evidently we were studying not simply a population which had at some time been poisoned by mustard gas, but a population poisoned by mustard gas and extensively affected by chronic bronchitis, either as a result of gassing or for other reasons.

It was, therefore, decided to investigate the mortality of soldiers from the 1914–18 war who on January 1, 1930, were being pensioned, and who were recorded as having bronchitis, but who had never been exposed to mustard gas. Ample material was available, but a limitation was imposed so that only individuals who had not served as soldiers overseas after the date of the first use of mustard gas were studied. This was necessary as there can be little doubt that many men exposed to small doses of the gas had no severe symptoms, and such cases would not be recorded in the Ministry's records as having been gassed.

Apart from this limitation, the choice from the available material relating to bronchitis cases without mustard gas exposure was made at random, and a series of 1,421 cases was studied.

It is of course possible that a man might be diagnosed as suffering from chronic bronchitis or a chest disability resulting from his war service when in fact he was suffering from an unrecognized lung cancer, which might later be correctly diagnosed. Thus a bias might exist because of the selective admission of lung cancer cases to the series, but this bias would be limited to cases dying in the first few years of the survey because of the limited survival time of sufferers from untreated cancer of the lung. Furthermore, it has already been stated that, although the survey starts in 1930 because this is the first year for which complete records are available, the men who were pensioned at that date had for the most part been pensioned or suffering from their disability for some time.

In order to gain some idea of how seriously a bias of this type might be affecting the findings discussed in this paper, the medical histories of those men in the mustard gas series or the bronchitis series who died of lung cancer within the arbitrary limit of 6 years from the starting date, January 1, 1930, were re-examined. Seven men in the mustard gas series and five in the bronchitis series fell into this category. This scrutiny revealed that in each of these cases the diagnosis of chronic bronchitis had been made as early as 1918. In fact, it appeared that all the cases of chronic bronchitis in these two series had been so diagnosed before the end of 1921. We therefore consider that the possibility of a bias due to the selective admission of lung cancer sufferers to the series under the mistaken diagnosis of chronic bronchitis can be ignored in assessing the results of these studies.

All the men in the two series so far considered were by definition serving soldiers in the 1914–18 war. This in itself might mean that the standards used, derived from the whole of the male population of England and Wales, might not be applicable to men selected in this way. From the time of their enlistment until they left active service, the men were presumably selected for physical fitness and the absence of any obvious sign of disease, and it might be thought that this would affect their subsequent mortality experience. There is also a widespread belief that members of the armed forces in the 1914–18 war smoked to excess (the colloquial term "gasper" originated at this time). Any analysis of the incidence of cancer of the lung and pleura might therefore be open to the objection that there would be a systematic bias in respect of smoking habits.

Whilst it is highly desirable that such a bias should if possible be excluded, or at least detected, the composition of the general population used for forming the standard of comparison must be considered. Of the cases studied, 70 per cent. were between the ages of 20 and 35 in 1917.

The Registrar-General's (1927) population estimates (Decennial Supplement, 1921) show that 58 per cent. of males in these age groups were in the armed forces in 1917, and the method used ensures that the mortality experience at any given date is the experience of these men as they pass through life. Thus the discrepancy between the armed forces and the general population is not so extreme as might be imagined.

Nevertheless, we thought it advisable to analyse a further sample of men drawn from the armed forces in 1914–18, who had not been exposed to mustard gas and who were not selected for bronchitis, although they might reasonably be assumed to develop it at a rate comparable with that in the general population. Ideally, such a series would consist of men who had served in the 1914–18 war, had not been exposed to mustard gas, and had been discharged from the forces without any obvious medical abnormality, but the Ministry of Pensions and National Insurance obviously do not keep such records.

A reasonable approximation to such a series, and one that was readily available, was found amongst men who had served in the 1914–18 war, had been wounded in a manner that necessitated a single leg amputation, and left France before July 12, 1917 (thus excluding unrecorded poisoning by mustard gas), and were receiving a pension for the disability of single-leggedness in 1930. A random selection of 1,114 such cases was made from the available data.

The method of statistical analysis adopted, the technical details of which are discussed in an appendix, allowed us to study both the number of deaths from each disease classification that were found (and that would be expected if the rates of death acting on the general population were also acting on each series of cases) and also the age at which these deaths took place. A study of age-incidence in human cancer is desirable, because few data exist to help elucidate how far the biological age of the host is important and how far the length and the subsequent period of exposure to outside inflences is important. This form of analysis has therefore been applied to each disease classification and to each series.

Results

The records of all the men in each series were examined, and the following information was extracted:

(*a*) age;
(*b*) whether alive or dead;
(*c*) if dead, date of death;
(*d*) if dead, cause of death.

In all cases where death had occurred, the death certificate was scrutinized, and the category to which the Registrar-General had assigned the death was determined. This was done since all the standard rates are based on deaths assigned to the disease classifications named; a death certificate might mention more than one disease, but be assigned to the category of only one of these.

Calculations were made from these data and from the analytical tables, and the expected numbers of deaths from all causes and in each of the disease classifications studied were determined. "Expected" in this context means the number that would have occurred had the mortality that affects the general population, defined as the male population of England and Wales, acted with the same severity in the series studied. These expected numbers and the mortality ratio (M.R.), which is defined as the number of "deaths found" expressed as a percentage of the number of "deaths expected", are shown in the Table. The mortality ratio for deaths from all causes is here calculated from Tables which allow the population to be depleted at the standard rates for England and Wales. Where the mortality ratio for "deaths from all causes" is markedly raised, the calculation of mortality ratios for individual diseases will be biased, since the actual number of years lived at each age period will become progressively less than the theoretical number as the population is

TABLE

MORTALITY FROM EACH CLASS OF DISEASE FOUND AND EXPECTED IN THREE SERIES STUDIED

Source of Data		Disease Class								
		All Causes		All Neoplasms		Cancer of Lung and Pleura		Neoplasms other than Cancer of Lung and Pleura		
		Deaths	Mortality Ratio	Deaths	Mortality Ratio	Deaths	Mortality Ratio	Deaths	Mortality Ratio	
Series	Mustard Gas	547	153* (VHS)	79	130 (S)	29	207 (HS)	50	107 (NS)	Found
		357·3		60·8		14·0		46·8		Expected
	Bronchitis	932	138* (VHS)	104	109 (NS)	29	201 (HS)	75	93 (NS)	Found
		673·8		95·0		14·4		80·6		Expected
	Amputation	383	105* (NS)	72	100 (NS)	13	84 (NS)	59	104 (NS)	Found
		365·7		72·2		15·5		56·7		Expected

VHS = very highly significant ($P < 0·0001$). HS = highly significant (P between 0·01 and 0·0001).
S = significant (P between 0·05 and 0·01). NS = not significant ($P > 0·05$).
*Mortality ratios based on theoretical number of years lived.

depleted by the excessive mortality. In the present study a complete statement of mortality has been made, and from this the actual number of years lived at each age period can be calculated. The mortality ratios for the classes of neoplastic disease have been calculated from this actual life experience.

In the Figure, where the age-distribution of deaths is shown, all the results have been calculated from the actual life experience, since the theoretical attenuation would tend to bias the results where the mortality ratios for "deaths from all causes" is high.

MUSTARD GAS SERIES.—In the mustard gas poisoning series, 1,267 men were alive on January 1, 1930, and between that date and December 31, 1952, 547 deaths had occurred, leaving 720 men still alive. The total number of deaths expected was 357, so that an excess of 190 deaths was found, the mortality ratio being 153. This difference is statistically very highly significant.*

*See Table for definition of significance levels, and for the rates from which the ratios are calculated, since these rates have been rounded off to whole numbers in the text.

Deaths from Neoplasm.—79 were found, and 61 expected, an excess of eighteen deaths, the mortality ratio being 130. This difference is statistically significant.

When these deaths are sub-divided into deaths from "cancer of the lung and pleura" and deaths from "neoplasms other than cancer of the lung and pleura", it is seen that the excess deaths from neoplasm can be attributed to a large excess of deaths from cancer of the lung and pleura. In this disease classification, 29 deaths were found and fourteen expected, giving an excess of fifteen and a mortality ratio of 207. This difference is statistically highly significant.

Fifty deaths from "neoplasms other than cancer of the lung and pleura" were found, and 47 expected. This is an excess of three deaths and a mortality ratio of 107. This difference is not statistically significant, in fact, the numbers expected and found are in very close agreement.

Finally, deaths from bronchitis were investigated, and it was found that 217 deaths classified as due to

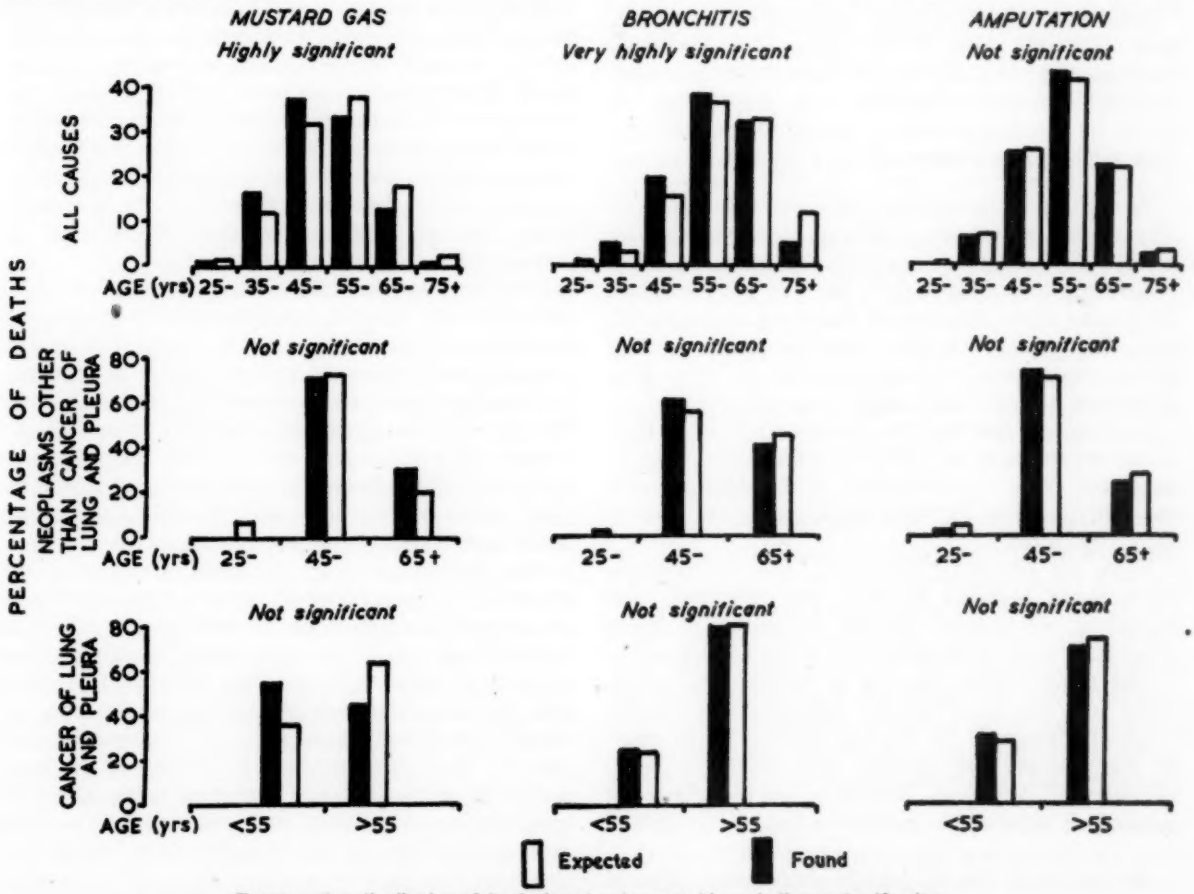

FIGURE.—Age distribution of deaths found and expected in each disease classification.
Not significant, $P > 0{\cdot}05$. Highly significant, $0{\cdot}01 > P > 0{\cdot}001$. Very highly significant, $P < 0{\cdot}0001$.

bronchitis (all types) had occurred as against 21 expected. This is a statistically very highly significant excess of 196, the mortality ratio being 1,033. This excess of 196 deaths could wholly account for the excess of 172 deaths left after the excess of neoplasm deaths had been taken into account. There remain 251 deaths from causes other than bronchitis or neoplasm, the expected number being 276. This deficit of 25 deaths is not statistically significant ($P = 0{\cdot}1$).

Considering the Figure showing the observed and expected frequency (as a percentage of the total deaths considered), the pattern of the age-specific mortality (*i.e.* percentage age distribution of deaths) from all causes is seen to have been altered, being relatively higher in younger age groups. This difference is statistically highly significant. Deaths from neoplasms other than cancer of the lung and pleura do not show this altered pattern, and although there is a suggestion that deaths from cancer of the lung and pleura do show such an effect, the difference is not statistically significant.

Bronchitis Series.—In this series 1,421 men were alive in 1930, and 932 deaths had occurred by December 31, 1952, leaving 489 survivors. The total number of deaths expected was 674, giving an excess of 256 deaths with a mortality ratio of 138. This difference is statistically very highly significant.

Deaths from Neoplasm.—104 were found, and 95 expected, an excess of nine and a mortality ratio of 109. This difference is not statistically significant.

Splitting these deaths into the two sub-divisions, 29 deaths from "cancer of the lung and pleura" were found and fourteen expected, an excess of fifteen deaths and a mortality ratio of 201. This difference is statistically highly significant.

Seventy-five deaths from "neoplasms other than cancer of the lung and pleura" were found, and 81 expected. This is a deficiency of six deaths and a mortality ratio of 93. This difference is not statistically significant.

Since the object of this work was to study the relationship between mustard gas poisoning and neoplasia, no detailed studies on causes of death other than from neoplasms were made on this series.

The Figure shows that, as in the previous series, there is a tendency for the age-specific mortality from all causes to be disproportionately increased in the younger age groups, this difference being statistically significant. Neither of the two classes of neoplasms show any significant effect of this sort.

AMPUTATION SERIES.—1,114 men were alive in 1930, and by December 31, 1952, 383 deaths had occurred, leaving 731 survivors. 366 deaths were expected, and an excess of seventeen deaths were found, the mortality ratio being 105. This difference is not statistically significant.

Deaths from Neoplasm.—72 were found and 72 were expected. The mortality ratio is therefore 100.

Thirteen deaths from "cancer of the lung and pleura" were found and sixteen expected. This deficiency of three* (mortality ratio 84) is not statistically significant.

59 deaths from "neoplasms other than cancer of the lung and pleura" were found and 57 expected. This excess of two* (mortality ratio 104) is not statistically significant.

The Figure shows no statistically significant alteration of the age-specific mortality pattern in any of the disease classes.

DISCUSSION

The foregoing results show that both the men who had been poisoned with mustard gas (and who nearly all suffered from bronchitis) and the men who suffered from bronchitis but were not poisoned with mustard gas, showed a very high general mortality. In the mustard gas series the excessive mortality could be completely accounted for by an excessive number of deaths from bronchitis and, to a lesser extent, by an excessive number of deaths from cancer of the lung and pleura. The reason for the excessive general mortality was not sought for in the bronchitis series, but an excessive number of deaths from cancer of the lung and pleura was found.

In both cases the deaths from cancer of the lung and pleura occurred at twice the rate for the general population. Deaths from other forms of neoplasia occurred at the same rate as in the general population.

The amputation series showed no deviation from the rates for the general population in any of the criteria studied, and so confirm that the standards derived from the general population can be used on these series of men who were by definition serving soldiers in the 1914–18 war.

The finding of a high incidence of cancer of the lung and pleura in both the mustard gas series and the bronchitis series does not support the view that mustard gas has acted as a direct carcinogen, but it does provide evidence that chronic bronchitis can be associated with an increased number of deaths attributed to carcinoma of the lung and pleura. This view has been advanced in the past, and some evidence for it published, especially with reference to bronchitis and the squamous-celled type of carcinoma of the bronchus (Lea, 1952).

*These figures do not exactly balance owing to rounding-off to whole numbers (See Table).

Unfortunately the Ministry of Pensions records do not contain histological findings, but it is proposed to attempt to obtain the pathological material from the hospitals concerned and to review the histopathology of the series.

It is of course a matter of common knowledge that diagnostic errors affect mortality rates based on death certificates. This topic has been discussed extensively by Kennaway and Kennaway (1936) and by Willis (1953). In the present studies most of these errors will affect the general population, the control series, and the two bronchitis series equally, and will not affect the conclusions. It only remains to consider whether there is a common factor in the mustard gas series and the bronchitis series which might systematically bias the diagnosis of cancer of the lung and pleura, and which will not be operating in the amputation series. A history of chronic chest disease, present by definition in the mustard gas and bronchitis series, might well be such a factor, but it is not obvious which way any bias from this source would work.

It might be argued that the pre-existing chest disease would cause more careful and more frequent examination of the respiratory system, with a consequent picking out of cases of malignant disease which would otherwise be missed, or it might be argued that more frequent incorrect diagnoses of lung cancer might be made because of the misinterpretation of abnormal physical signs due to the underlying chronic condition. Both these sources of error would tend to give an increase of the number of cases found compared with the number expected, but, if they do operate to any extent, it is somewhat surprising that a connexion between chronic chest disease and lung cancer is not well recognized by diagnosticians, since both would presumably operate amongst the chronic bronchitics in the general population.

On the other hand, it might plausibly be argued that a chronic chest lesion would lead to a diminished tendency to diagnose malignant disease of the lung, since it is not commonly thought that lung cancer is associated with a long history or is compatible with a long survival time in an untreated state; since superimposed physical signs due to the development of carcinoma in a chronically diseased lung might easily be missed against the pre-existing background of abnormality; and since clinical teaching discourages the diagnosis of a double pathology.

These questions cannot be resolved by the present studies, but the different possibilities presented should be borne in mind. The authors' opinion inclines to the possibility of underdiagnosis of lung cancer rather than to its overdiagnosis in the two bronchitic series.

If we accept that the excess of cancer of the lung and pleura in the two bronchitic series is real and also has a common aetiological factor in the bronchitis, the cancer experience of both groups can be pooled and used to examine a hypothesis advanced by Cramer (1936):

> There appears to be a general law that when in a given population the incidence of cancer in one particular organ is markedly increased as compared with another population, then there is a compensating decrease in the incidence of cancer in a number of the other organs. As a result, the incidence of cancer in different populations, whether of the same sex or not, may be composed of a very different distribution over the various organs or tissues, but the sum total, the total incidence of cancer, remains on an even level.

This hypothesis seems to have been made into the implicit basis of recent speculation in relation to the smoking and lung cancer problem (Blond, 1954; Price Thomas, 1955). Possibly by an extension of the original intended scope of Cramers' "law", they suggest that the excess of lung cancer in tobacco smokers reported by (amongst others) Doll and Bradford Hill (1952, 1954) does not mean that cancer is being induced, but that the site where it becomes manifest is determined by the effect of smoking.

In the two bronchitic series studied, 58 deaths from cancer of the lung were found and 28 expected. If the increase in this site is being compensated for by a decrease in cancer of other sites, as required by the hypothesis extended in the sense required by the speculations about smoking, then there should be a deficit of about thirty cases of death from neoplasm other than cancer of the lung and pleura. In fact 125 are found and 127 expected. This close agreement does not support the view that Cramer's "law" is valid in this case.

Summary and Conclusions

(1) We have made an examination of the mortality experience of 1,267 war pensioners who suffered from mustard gas poisoning in the 1914–18 war, and who were still alive on January 1, 1930. It was found that almost all (over 80 per cent.) had chronic bronchitis at that date. In subsequent years a statistically significant excess of deaths attributed to cancer of the lung and pleura has been observed amongst them (29 deaths found compared with fourteen expected).

(2) A similar and statistically significant excess of deaths attributed to cancer of the lung and pleura was found amongst a series of 1,421 war pensioners

who served in the 1914–18 war, and suffered from chronic bronchitis, but had never been exposed to mustard gas (29 deaths found compared with fourteen expected).

(3) No statistically significant difference between the number of deaths from cancer of the lung and pleura found and expected was detected in a series of pensioners from the 1914–18 war who were receiving a pension because of having had one leg amputated, who had never been exposed to mustard gas, and whose inclusion in the series was independent of any selection for chronic bronchitis (thirteen deaths found compared with sixteen expected).

(4) No statistically significant difference between the number of deaths from neoplasms other than cancer of the lung and pleura found and expected was detected in any of the three series.

(5) The possibility that a systematic bias might arise from analytical tables based on a general population of all males in England and Wales being inapplicable to a series of men who were by definition serving soldiers in the 1914–18 war has been excluded, and the possibility of a diagnostic bias considered and discussed.

(6) The evidence presented does not support the view that mustard gas has acted as a direct carcinogen, either in relation to neoplasia in general or in relation to cancer of the lung and pleura.

(7) The evidence indicates that chronic bronchitis may be associated with the subsequent development of cancer of the lung and pleura, unless it is assumed that the excess of deaths attributed to this disease is entirely due to diagnostic bias.

(8) The increased incidence of cancer of the lung and pleura, whether real or apparent, in the pooled data derived from the cases of mustard gas poisoning, nearly all of whom were also suffering from chronic bronchitis, and from the cases of chronic bronchitis who had not been exposed to mustard gas, was not compensated for by a diminution of mortality from neoplasms other than cancer of the lung and pleura.

We should like to thank Professor R. V. Christie, Dr. R. Doll, Professor A. B. Hill, F.R.S., and Professor Sir Ernest Kennaway, F.R.S., for raising certain questions for our consideration and discussion, and the Registrar-General's staff for helping in tracing and checking the allocation of death certificates to the various disease categories.

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STATISTICAL APPENDIX

Methods of Analysis and Detailed Results

Comparative composite cohort analysis, the method that has been used in these studies, is a technique for comparing some or all of the morbidity or mortality experience of a "closed" and defined population with an expected experience calculated for that population at some standard rate. A "closed" population is one in which the whole of the life experience of each of its members, subsequent to the entry of that member into the observational field, is of relevance to the analysis, regardless of whether or not the member has ceased to belong to the particular defined class (*e.g.* environmental, occupational, or industrial) which was used in circumscribing the observational field when designing the survey. This concept is in contrast to the "open" population, such as is necessarily used in the

Registrar-General's studies in occupational mortality (*e.g.* Registrar-General, 1938), where an estimate of the population in a stated environment in a given year or series of years is used, but where the member must be allocated to that environment on the death or sickness certificate for his experience to be used. This allows members who enter the observational field to leave it subsequently by changing their allocated environment, and only their life experience whilst still allocated to the environment which causes them to be classified in the observational field of the survey is relevant to the analysis.

The essential nature of the technique has been further discussed by Case and Hosker (1954), and a specific example of a method of deriving a standard rate for male mortality from bladder tumour in England and Wales is given by Case (1953a, b).

From a practical viewpoint, the method requires a statement of the years of life experienced at different ages, since both morbidity and mortality are highly age-specific, and these experiences must be calculated so that allowance is made for the date to which the age experience refers, since contemporaneous conditions also affect morbidity and mortality. Once the statement of the life experience differentiated in this way is made, the morbidity or mortality to be expected under some defined standard conditions can be calculated by applying morbidity or mortality rates calculated for the age and date from data relating to the standard conditions. The sum of the expectation of experience over the whole array then gives the mortality or morbidity expected, and this can be compared with that observed.

In order to facilitate the study of environmental factors affecting neoplastic disease, Case and Pearson (work in progress) are preparing Tables for mortality experience in England and Wales from 1911 onwards. These will be calculated with respect to 5-year age grouping, *e.g.* 35– 40– 45– etc., and 5-year date grouping, *e.g.* 1911–, 1916–, 1921–. Thus the rate applicable to members of a cohort of men born in 1866–1869 will be found under 45– and 1911–, 50– and 1916–, and so on. These Tables, calculated for each sex separately, will cover the ${}_5q_x$ values of the Life Table, mortality rates from all causes, and mortality rates for neoplastic disease under 24 site-headings distinguishable since 1911.

In the present study, the mortality Tables for males in England and Wales for death from all causes, death from "all neoplasms" (as defined in the text), death from "cancer of the lung and pleura", ${}_5q_x$ Life Table values, and a specially computed Table for deaths from "bronchitis, all types" were used.

Since the data to be studied contain a complete statement of mortality, the actual life experience differentiated for age and date can be computed fairly accurately, and is therefore used where applicable.

The calculation is intricate but of general interest. We therefore give the details for the mustard gas series *in extenso* in Columns 1 to 9 of Appendix Table A (overleaf) as a "worked example". Columns 10 and 11 show the results of calculations made in the same way for the bronchitis series and the amputation series respectively.

The calculations may conveniently be arranged in a "staircase" array (see Table A), so that a diagonal line traced from Column 2 to Column 7 will follow a cohort of men born in the same quinquennium. This type of array has the advantage that a lateral summation of Columns 2 to 7 gives the expected age distribution of the deaths.

Two methods may be used to calculate the life experience in each cell. The first is the theoretical attenuation, but in this case this is only used when considering the expected mortality for all causes. The calculation is made by taking the figure in the *a* division of Column 2 and multiplying this by the appropriate ${}_5q_x$ value of the Life Table. Since Column 2 relates only to one year, 1930, the result is divided by 5, since the ${}_5q_x$ value refers to a 5-year period. This gives the number of deaths expected, and is entered in the *b* division. This number is subtracted from the figure in the *a* division, and the result transferred to the *a* division of Column 3, in the next highest age group. This process is repeated across the whole of Table A, except that in Columns 3 to 6 no division by 5 is required, and that in Column 7 the division is by 2·5. A cross summation gives the age distribution expected, and the sum of this column gives the number of deaths expected. The observed deaths are entered in the appropriate cells, and summated similarly for comparison.

The numbers of deaths from all causes, found and expected, for each series studied, are shown in the *b* divisions of Table A. The expected age distribution calculated on this basis is shown in Column 9, but the progressive departure of the theoretical attenuation from the factual attenuation render them unsuitable for use in the text Figure, although the final total is appropriate for consideration in respect of the mortality ratio.

If it were necessary to obtain the theoretical life experience in each cell, this could be done by dividing the expected number of deaths in each cell by the appropriate age-specific death rate from all causes. In the present studies the actual life experience can be determined fairly accurately by multiplying the

APPENDIX TABLE A

1,267 CASES OF MEN OF THE 1914–18 WAR WHO HAD BEEN POISONED BY
COMPARATIVE COMPOSITE COHORT ANALYSIS ARRAY TO ANALYSE FOR DEATHS FROM ALL CAUSES, DEATHS FROM
FROM NEOPLASMS OTHER THAN CANCER OF THE LUNG AND PLEURA, WITH AGE DISTRIBUTIONS

Column	1	2				3				4				5				6			
Rank	Age	Date																			
1		1930				1931–				1936–				1941–				1946–			
2	25–	89	0	0	0																
			0·31	0·01	0·00																
3	30–	388	1	0	0	89	4	0	0												
			1·48	0·08	0·00		1·53	0·10	0·01												
4	35–	331	4	0	0	387	22	0	0	85	7	0	0								
			1·71	0·11	0·01		8·82	0·69	0·10		1·83	0·15	0·03								
5	40–	259	1	0	1	327	24	0	0	365	22	0	0	78	9	0	0				
			1·82	0·16	0·01		10·08	0·99	0·14		10·81	1·14	0·27		2·26	0·22	0·07				
6	45–	150	1	0	0	258	25	1	1	303	19	3	2	343	29	2	2	69	5	0	2
			1·44	0·17	0·01		11·64	1·44	0·23		13·46	1·58	0·40		13·71	1·66	0·63		2·74	0·36	0·19
7	50–	46	0	0	0	149	10	1	0	233	30	2	1	284	38	4	5	314	38	3	2
			0·60	0·10	0·01		9·48	1·51	0·19		16·08	2·16	0·47		17·64	2·32	0·79		18·47	2·48	1·41
8	55–	4	2	0	0	46	6	0	0	139	22	2	0	203	32	1	3	246	31	2	0
			0·08	0·01	0·00		4·19	0·77	0·07		13·35	2·14	0·37		21·25	2·81	0·83		24·11	3·34	1·57
9	60–					2	2	0	0	40	6*	0	0	117	13	4	1	171	35	4	1
							0·53	0·03	0·03		5·89	1·04	0·12		16·63	2·79	0·57		28·70	3·52	1·31
10	65–									0	0	0	0	34	6	0	0	104	29	6	1
											0·70	0·00	0·00		6·86	1·26	0·15		20·72	3·12	0·77
11	70–													0	0	0	0	28	8	0	0
															0·75	0·00	0·00		8·19	1·37	0·18
12	75–																	0	0	0	0
																			0·79	0·00	0·00
13	80–																				
14	85+																				
15		*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*	*a*	*b*	*c*	*d*
	Total	1,267																			

a = men surviving to start of date period
b = deaths from all causes
c = deaths from neoplasms other than cancer of lung and pleura
d = deaths from cancer of lung and pleura
* = corrected for continuity
Dotted lines indicate cells combined for χ^2 test

MUSTARD GAS
CANCER OF THE LUNG AND PLEURA, AND DEATHS OF DEATH IN EACH CLASS

7				8	9			Results from Analysis of 1,421 Cases of Bronchitis in Men not Exposed to Mustard Gas			Results from Analysis of 1,114 Cases of Single Leg Amputation in Men not Exposed to Mustard Gas			12
1951 and 1952				Alive on January 1, 1953	Age Distribution of Deaths Σ Columns 2 to 7			Age Distribution of Deaths			Age Distribution of Deaths			
					0	0	0	0	0	0	—	—	—	Found
					0·31	0·01	0·00	0·02	0·00	0·00	—	—	—	Expected
					5	0	0	0	0	0	0	0	0	Found
					3·01	0·18	0·01	0·64	0·04	0·00	0·80	0·04	0·00	Expected
					33	0	0	9	0	2	7	0	0	Found
					12·36	0·95	0·14	4·52	0·34	0·05	6·69	0·50	0·07	Expected
					56	0	1	36	0	0	16	1	0	Found
					24·97	2·51	0·49	12·95	1·27	0·20	19·11	1·97	0·32	Expected
					79	6	7	66	2	3	36	8	0	Found
					42·99	5·21	1·46	29·44	3·47	0·77	36·26	4·62	1·12	Expected
64	3	1	0	61	119	11	8	119	7	1	62	7	4	Found
	1·69	0·21	0·15		63·96	8·78	3·02	56·46	7·92	1·90	58·09	8·81	2·63	Expected
276	16	2	3	260	109	7	6	161	21	5	86	14	4	Found
	11·52	1·49	1·00		74·50	10·56	3·84	93·32	13·96	3·26	77·10	12·73	4·30	Expected
215	15	3	4	200	71	11	6	191	15	5	81	15	2	Found
	14·35	1·83	0·94		66·10	9·21	2·94	123·46	17·98	3·55	75·57	12·73	3·93	Expected
136	14	6	0	122	49	12	1	184	16	9	62	11	2	Found
	15·60	1·74	0·66		43·88	6·12	1·58	167·10	17·42	2·75	53·30	8·97	2·19	Expected
75	15	2	0	60	23	2	0	113	11	3	24	2	1	Found
	10·56	1·36	0·30		19·50	2·73	0·48	103·16	11·09	1·24	28·69	4·65	0·75	Expected
20	3	1	0	17	3	1	0	40	3	1	8	1	0	Found
	3·51	0·55	0·67		4·30	0·55	0·07	57·45	5·21	0·46	9·18	1·52	0·16	Expected
0	0	0	0	0	0	0	0	11	0	0	1	0	0	Found
	0·27	0·00	0·00		1·42	0·00	0·00	21·31	1·68	0·18	0·94	0·15	0·01	Expected
					—	—	—	2	0	0	—	—	—	Found
					—	—	—	3·89	0·21	0·02	—	—	—	Expected
a	*b*	*c*	*d*		*b*	*c*	*d*	*b*	*c*	*d*	*b*	*c*	*d*	
				Total = 720										

Total found ..	547	50	29	932	75	29	383	59	13		
Total expected ..	357·30	46·81	14·03	673·82	80·59	14·38	365·73	56·69	15·48		
Difference ..	189·70	3·19	14·97	258·18	5·59	14·62	17·27	2·31	2·48		
P	<0·0001	0·6	0·005	<0·0001	0·5	0·008	0·4	0·8	0·5		
Difference of Distribution	χ^2	42·15	5·77	3·60*	106·86	8·75	0·04*	3·54	3·09	0·31*	
	n	8	4	1	10	6	1	8	5	1	
	P	<0·0001	0·2	0·06	<0·0001	0·2	0·85	0·9	0·7	0·6	

APPENDIX TABLE B

NUMBER AND AGE DISTRIBUTION OF DEATHS FROM ALL CAUSES CALCULATED FROM ACTUAL NUMBER OF YEARS LIVED AT EACH AGE PERIOD

Source of Data			Age Period											Mortality Ratio	Difference of Distribution
			<35	35–	40–	45–	50–	55–	60–	65–	70–	75+	Total		
Series	Mustard Gas	Found	5	33	56	79	119	109	71	49	23	3	547	173	$\chi^2 = 32{\cdot}86$ $n = 9$ $P < 0{\cdot}001$
		Expected	3·31	12·13	23·87	40·27	57·78	64·28	55·16	36·66	17·68	4·28	315·42		
	Bronchitis	Found	0	9	36	66	119	161	191	184	113	53	932	184	$\chi^2 = 53{\cdot}13$ $n = 8$ $P < 0{\cdot}0001$
		Expected	0·67	4·23	12·47	27·46	51·87	81·34	100·45	97·60	68·59	61·92	506·60		
	Amputation	Found	0	7	16	36	62	86	81	62	24	9	383	103	$\chi^2 = 5{\cdot}24$ $n = 8$ $P = 0{\cdot}7$
		Expected	0·80	6·68	19·27	36·38	58·29	76·88	75·86	53·29	29·63	13·16	370·26		

Dotted line indicates cells combined for χ^2 test.

number of survivors of each column by the number of years that the column refers to, and then adding the actual number of years lived in the period by those who have died on the assumption that each death took place in the middle of the year. Thus a person dying in 1943 would be regarded as having lived 2·5 years in the period 1941–44.

The number of deaths expected for each disease classification to be considered can then be determined by multiplying the years of life lived by the appropriate age specific death rate for that disease classification. The expectations for cancer of the lung and pleura and for neoplasms other than cancer of the lung and pleura with the figures actually found, are shown in the *d* and *c* divisions of Tables A and B. The age distributions, being calculated from the factual attenuation, are suitable for use in the text Figure.

The expected age distribution for deaths from all causes, based on the factual attenuation, has been separately calculated for use in that Figure, and is shown in Appendix Table B.

The significance of differences of totals has been assessed by the approximation used by the Registrar-General (1949) of regarding the square root of the number of deaths found as the standard error. The *P* value is then determined from Tables of the normal curve from the observed difference between the expectation and the number found over the square root of the number found.

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INJURIES IN THE AGED

BY

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Persons over 65 years of age now comprise 11 per cent. of the population. This proportion is rising; 50 years ago it was 5 per cent., and it is estimated that in 50 years' time it will be 17 per cent. (Logan, 1953). Correspondingly, the medical and surgical needs of the elderly are demanding increasing attention. It is common to find one-third of the beds in accident wards occupied by these people, and it therefore seemed profitable to define more precisely what kinds of injuries are chiefly concerned, how they happen, and what are their results in mortality, duration of stay in hospital, and resettlement problems.

Patients

Two main sources of information have been studied: general statistics for the whole of Birmingham, and details of cases treated at the Birmingham Accident Hospital. The general statistics were derived from an analysis of all in-patients aged 65 or more, who were discharged during 1952 from Birmingham hospitals and resided within the city boundary. From the Accident Hospital, details were obtained directly from the case-notes of in-patients over 65. A sample was also taken of all new attendances at the hospital (both in-patients and out-patients).

The total number of Birmingham residents over 65 years receiving in-patient treatment for injuries in the year was 849, of whom 491 were treated at the Accident Hospital.

Sample of All Elderly Patients coming to the Accident Hospital.—A 6-month sample, taking alternate months, showed that approximately 2,400 of all patients (50,620) who attended the Accident Hospital for the first time in 1952 were over 65 years of age. Of these, 604 (including 491 Birmingham residents) were admitted as in-patients, 183 remaining for one day only. The following analyses are based on 500 cases selected at random from the original 6-month sample.

38 per cent. of persons in this group were under the age of 70 and 30 per cent. were over 75 years. Lacerations, contusions, and strains accounted for 41 per cent. of the injuries and fractures for a further 39 per cent. Less than 2 per cent. were cases of osteo-arthritis, either caused or aggravated by trauma (Fig. 1).

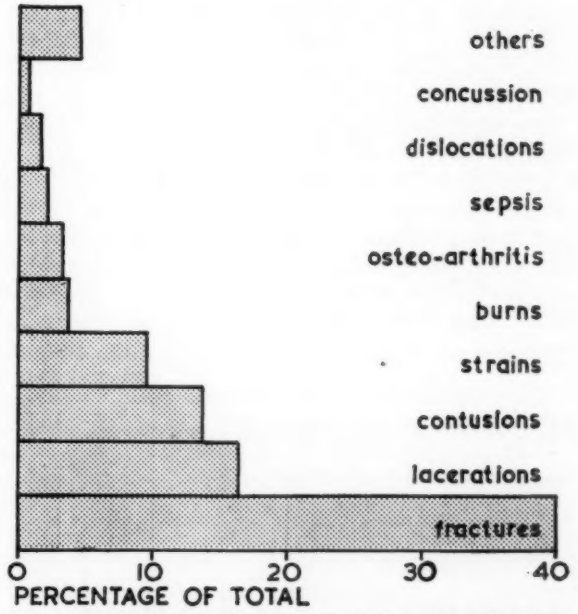

Fig. 1.—Distribution according to diagnosis of sample of all patients over 65 years of age admitted to the Accident Hospital in 1952, expressed as percentages of total sample.

Of the fractures, 48 per cent. were of the upper and 39 per cent. of the lower limbs (Table I, overleaf). Fractured radius and ulna (including Colles fractures) constituted 30 per cent. of all fractures, and fractured femurs 16 per cent. As will be shown later the

TABLE I

SITES OF FRACTURES IN THE ELDERLY (SAMPLE OF ALL BIRMINGHAM ACCIDENT HOSPITAL ADMISSIONS, INCLUDING OUTPATIENTS)

Site		No. of Patients	Percentage of all Fractures
Upper Limb ..	Colles and wrist..	38	19·2
	Radius and ulna	22	11·1
	Hands and fingers	17	8·6
	Humerus.. ..	18	9·1
	Total	95	48·0
Lower Limb ..	Femur	32	16·2
	Tibia and fibula..	15	7·6
	Feet and toes ..	6	3·0
	Ankle	20	10·1
	Patella	4	2·0
	Total	77	38·9
Trunk and Head	Ribs and sternum	10	5·1
	Head and face ..	4	2·0
	Clavicle	2	1·0
	Pelvis	2	1·0
	Total	18	9·1
Others		8	4·0
Total		198	100

lower-limb fractures, though less in numbers, are much more important in mortality and in causing confinement to bed and inconvenience at home.

Division of the accidents by circumstance of occurrence (Table II) revealed a preponderance of domestic accidents (57 per cent.) with road and transport accounting for 25 per cent. and industrial accidents for 13 per cent. Two-thirds of all the injuries were due to falls and in only thirty of the 123 road accidents was the patient knocked down by a moving vehicle. Of the twenty burns, seventeen were domestic and three industrial. As in a previous survey (Colebrook and Colebrook, 1951) domestic burns were more frequent among women than men.

In the analysis of treatment times (Table III, opposite) patients were divided into three categories:

(1) Attended casualty department once;
(2) Attended out-patients department more than once;
(3) In-patients.

Fractures had the longest period of out-patient treatment (11 weeks), and lacerations the shortest (2 weeks), apart from one patient with concussion. Strains and dislocations had mean out-patient treatment times of 8 and 9 weeks respectively, during which time many of the patients were attending the rehabilitation department. The mean treatment time for all injuries treated only in out-patients was 7 weeks. In all treatment times, those dying were not included, since this would give misleading values. Of the 89 in-patients, 59 (66 per cent.) returned as out-patients. The remainder included six fatalities in hospital and 24 persons who were transferred either to other institutions or to their general practitioners. One case of burns attended out-patients for 32 weeks; 47 fractures averaged 18 weeks, and the remaining eleven cases less than 2 weeks.

All Birmingham In-patients.—The records of all Birmingham hospitals included 849 patients over 65 years old who were discharged from the wards during 1952, after treatment for injuries. These cases comprise almost all the severe injuries occurring among the 104,297 persons over 65 years of age resident in the City (Census 1951, 1954). Their diagnoses, recorded according to the International Statistical Classification of Diseases and Causes of Death (W.H.O., 1948) were grouped for convenience as in Table IV, opposite. Fractures were by far the most common cause of admission, accounting for about two-thirds of the cases, and among them fractured femurs were the most frequent and

TABLE II

CIRCUMSTANCES OF ACCIDENTS IN THE ELDERLY (SAMPLE OF ALL BIRMINGHAM ACCIDENT HOSPITAL ADMISSIONS INCLUDING OUTPATIENTS)

Accidents	Industrial	Domestic	Road or Transport	Other	Total	
					No.	Per cent.
Fell on stairs or steps	1	40	1	1	43	8·6
Other falls	13	182	82	5	282	56·4
Hit by falling weight	10	5	0	0	15	3·0
Cut by tools, etc.	15	13	0	1	29	5·8
Knocked down by vehicle	0	0	30	0	30	6·0
Burned or scalded	3	17	0	0	20	4·0
Trapped or crushed	11	1	2	0	14	2·8
Strained (lifting heavy weights).. ..	4	2	3	0	9	1·8
Foreign body	2	3	0	1	6	1·2
Others	7	22	5	18	52	10·4
Total	66	285	123	26	500	100·0
Percentage	13·2	57·0	24·6	5·2		

TABLE III

ANALYSIS OF SAMPLE OF ALL ADMISSIONS, BY DIAGNOSIS, AND TYPE AND DURATION OF TREATMENT

Diagnosis	Out-Patients			In-Patients					Total	
	No. attending Once only	No. attending More than Once	Mean Duration of Treatment (wks)	No.	Mean Duration of Stay (days)	No. re-attending as Out-patients	Mean Duration of Out-patient Treatment (wks)	No. of Deaths	No.	Per cent.
Fracture	4	126	11	68	29	47	18	8	198	39·6
Laceration	19	59	2	10	17	6	4	0	88	17·6
Contusion	33	39	4	2	11	1	2	0	74	14·8
Strain	16	34	8	1	4	1	4	0	51	10·2
Burn	4	15	5	1	112	1	32	0	20	4·0
Osteo-arthritis ..	6	10	5	1	1	1	2	0	17	3·4
Sepsis	0	12	3	0	0	0	0	0	12	2·4
Dislocation	2	9	9	0	0	0	0	0	11	2·2
Concussion	0	1	1	3	1	0	0	0	4	0·8
Others	16	6	3	3	6	2	5	2	25	5·0
Total	100	311	7	89	25	59	15	10	500	100·0
Percentage	20	62		18					100	

TABLE IV

DIAGNOSES, HOSPITAL STAY, AND MORTALITY OF ALL BIRMINGHAM IN-PATIENTS

International Statistical Classification	Diagnosis	No. of Patients	Mean Age (yrs)	Mean Duration In-patient Stay (days)	No. of Deaths	Case Mortality (per cent.)	Deaths as percentage of all Deaths due to Injury
800–4 850–6	Head injury	126	73·8	7	11	8·7	12·2
805–6	Fractured vertebral column	15	72·7	19	1	6·7	1·1
807–9	Fracture of pelvis and trunk	52	73·4	16	7	13·5	7·8
810–8	Fracture of upper limbs	113	73·1	9	2	1·8	2·2
820–9	Fracture of lower limbs	340	75·9	47	45	13·2	50·0
830–48	Dislocation, strain	33	75·4	5	0	0	0
870–929	Laceration, contusion, superficial injury	94	73·3	8	7	7·4	7·8
930–6 960–79	Foreign body and poisoning	35	71·2	8	6	17·1	6·7
940–9	Burn	24	73·4	39	8	33·3	8·9
985–98	Other or unspecified	17	75·8	3	3	17·6	3·3
Total		849	74·5	24·7	90	10·6	100·0

caused the longest stays in hospital. Burns, though less numerous, showed a long in-patient treatment time and had the highest case mortality. The mean age for all diagnoses (74·5 years) was roughly the same for all types of injury.

Among the 849 patients there were ninety deaths (a case mortality of 10·6 per cent.). The case mortality of fractured lower limbs (13 per cent.) was lower than that for burns (33 per cent.), but 50 per cent. of all accidental deaths were caused by the former (44 per cent. fractured femurs; 6 per cent. fractured tibia and fibula) as opposed to 9 per cent. due to burns. Bull and Fisher (1954) have recently reported a case mortality of 44 per cent. for 144 elderly patients admitted to a burns unit over a period of 10 years. For England and Wales in 1953, deaths caused by fractured lower limbs and burns represented 15 and 5 per cent. respectively of all deaths, while accidental deaths (other than suicides) increased from 0·4 per 1,000 for the 65–69 age group to 5·7 per 1,000 for persons over 85 years (Registrar-General, 1953). The corresponding figures for Birmingham (excluding cases not admitted to hospital) were 0·2 and 8·3 respectively.

The mean survival time showed considerable variation (Table V, overleaf). Thus the 17 days average for fatal head injuries ranged from 3 days for fractured skulls to 25 days for other head injuries. The longest mean time was 77 days for fractured femurs.

In Table VI (overleaf) the relationship between age and treatment time for the Birmingham in-patients is

TABLE V
PERIODS OF SURVIVAL OF BIRMINGHAM IN-PATIENTS SUSTAINING FATAL ACCIDENTS

Diagnosis	No. of Patients	Mean Age (yrs)	Mean Interval before Death (days)
Head injury	11	75·5	17
Fracture of trunk ..	8	78·5	18
Upper limb fracture ..	2	85·5	62
Fractured femur ..	40	80·7	77
Other lower limb fracture (tibia and fibula) ..	5	84·8	11
Laceration, contusion, superficial injury, etc.	7	77·6	8
Burn	8	75·5	25
Poisoning and others ..	9	74·0	5

TABLE VI
LENGTH OF IN-PATIENT TREATMENT FOR ALL BIRMINGHAM PATIENTS*

Age Group (yrs)	All Birmingham Patients		All Birmingham Patients with Fractured Femurs	
	No.	Mean Duration of Stay (days)	No.	Mean Duration of Stay (days)
65–69	201	21	43	59
70–74	201	20	42	50
75–79	198	22	57	52
80–84	113	38	47	75
85+	46	43	24	61
Total ..	759	25	213	59

* Patients who died are excluded.

considered (excluding deaths). Up to the age of 79 years the average stay in bed remained constant at 21 days. There was then a steady increase to an average healing time of 43 days for persons over 85. Mean stays for fractured femurs were far in excess of the overall values, and did not increase with age. A similar analysis of the Birmingham Accident Hospital in-patients confirmed these findings.

The total number of bed days for the one year's treatment of injuries in the elderly for all Birmingham hospitals, was 22,615 (including deaths); from this it can be estimated than 62 beds were occupied per day, 43 of them by patients with fractured femurs. Of the 42 beds occupied per day in Birmingham Accident Hospital by patients over 65 years, 30 were in use for patients with fractured femurs.

To relate the in-patient figures to the population of Birmingham, the numbers in each 5-year group were compared with the 1951 census (Fig. 2).

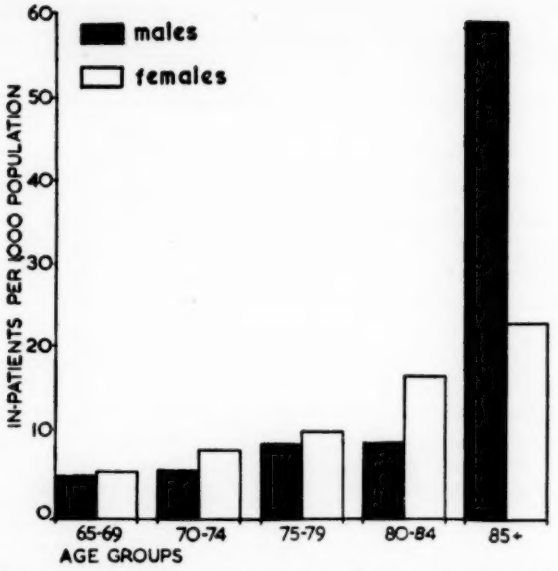

FIG. 2.—All accidents to persons over 65 years of age requiring in-patient treatment at Birmingham hospitals in 1952, related to population at risk.

There were almost twice as many females as males in the in-patient figures, whereas in the population at large the ratio was only 1·4 : 1. The excess of female in-patients increased steadily with age. For males a gradual increase in incidence for 65–84 years was followed by an abrupt rise after 85 years. Though the number of accidents on the road in this group is not great and is exceeded by females of the same age, the population in which they occur is very small.

Monthly admission rates showed a fairly even incidence from March to November followed by a period about 25 per cent. above the average from December to February. This winter peak is largely due to an increase in the number of road accidents, particularly falls on slippery surfaces.

Analysis of the Most Frequent Limb Fractures.—An estimate of the total number of certain types of fracture (femur, radius and ulna, and ankle) treated at the Birmingham Accident Hospital in 1952 is given in Table VII. All those who sustained a

TABLE VII
PATIENTS WITH FRACTURES OF FEMUR, RADIUS AND ULNA, AND ANKLE (BIRMINGHAM ACCIDENT HOSPITAL IN-PATIENTS AND SAMPLE TOTAL ADMISSIONS)

Site of Fracture	No. of Cases during Year	No. attending Out-patients only	In-patients staying One Day only	In-patients staying More than One Day	Mean Duration of Stay (days)	In-patients with Other Associated Injuries	Deaths
Femur	204	0	0	204	61	12	47
Radius and ulna (inc. Colles)	302	240	41	12	23	8	1
Ankle	124	86	12	26	21	4	0

fractured femur were admitted as in-patients, compared with only one-fifth of those with fractured radius and ulna, and one-third of those with fractured ankle. Two-thirds of the in-patients with fractured radius and ulna and one-third of the in-patients with fractured ankle stayed only one day for reduction under anaesthesia. The only death associated with fractured radius and ulna occurred in a man of 78 who also had compound fractures of the tibia, fibula, and humerus.

Patients sustaining more than one of these three types of fracture are classified in Table VII according to that judged to be the most serious. Thus, seven patients with fractured femur, radius and ulna were included under femur, and two with fractures of radius, ulna, and ankle were classified under ankle. Apart from the seven with fractured femur just mentioned, there were three who also had a fractured pelvis (two of whom died) and two with other fractures. Three of the eight patients with fractured radius and ulna also had fractured tibia and fibula, and one died after 2 days in hospital. A further three patients had fractured pelvis, and two had fractured humerus. All four of the patients with fractured ankle and additional injuries also had fractures of the upper limbs.

The circumstances of each accident were noted in order to determine the main causes of these arm, leg and ankle injuries; it was found that 69 per cent. of the fractures of the femur had been caused by domestic falls (*e.g.* downstairs, out of bed, over obstacles on the floor, and from windows). About two-thirds of the fractures of the radius and ulna, and one-half of the fractures of the ankle resulted from similar accidents. 23 per cent. of the fractures of the femur were sustained on the road, but only five patients had been knocked down by a moving vehicle; 33 per cent. of the fractures of the radius, ulna, and ankle occurred on the road, and in approximately one-third of each group the patients had been knocked down.

The mean stay in hospital of patients with these injuries did not increase markedly with age. The fractures of radius and ulna showed a diminishing duration of in-patient treatment with age, but this may have been due to selective admission. The case mortality for fractures of the femur increased with age (Table VIII), but the mean in-patient stay before death was variable.

TABLE VIII

MORTALITY AMONGST ALL BIRMINGHAM IN-PATIENTS WITH FRACTURED FEMURS

Age Group (yrs)	Mean Age (yrs)	No. of Deaths	No. of Patients	Mortality (Per cent.)	Mean Interval before Death (days)
65–69	68	2	45	4·4	22
70–74	71·4	8	51	15·7	104*
75–79	77·5	6	62	9·7	41
80–84	82·7	13	60	21·7	42
85+	88·8	11	35	31·4	19

* Another patient survived for 1,305 days.

SOCIAL PROBLEMS

About one-third (30·7 per cent.) of the in-patients at the Accident Hospital required the Almoner's assistance. Four main groups were encountered:

(1) Accommodation and domestic help.
(2) Financial aid.
(3) Home nursing equipment.
(4) Occupational adjustment.

(1) TROUBLE OVER DISCHARGE HOME.—This was due either to housing difficulties or to lack of suitable help in the home. Such patients were classified as follows:

(*a*) *Moderate Domestic Difficulties.*—Ultimately, most of these were suitably accommodated with friends or relations (32 per cent.).
(*b*) *Serious Domestic Difficulties.*—Those which prevented return home on discharge (34 per cent.).
(*c*) *Transferred to Infirmary or Nursing Home.*—This was mainly because the patient required further nursing treatment, and not because of social circumstances (4 per cent.).
(*d*) *Convalescence.*—These patients went for short periods of convalescence before returning home (6·5 per cent.).
(*e*) *Domestic Assistance.*—These patients returned home with the assistance of a home-help or district nurse (7·5 per cent.).

(2) FINANCIAL DIFFICULTIES.—These patients fell into two categories:

(*a*) Concerning the National Assistance Board or Ministry of National Insurance (6 per cent.).
(*b*) Concerning compensation as a result of the accident (1·5 per cent.).

(3) EQUIPMENT.—These patients needed such things as wheel chairs and other home-nursing equipment (4 per cent.).

(4) OCCUPATIONAL ADJUSTMENT.—This was sometimes required because the patient was unable to return to his pre-accident employment, and had to make arrangements to do some other suitable light work (4 per cent.).

Of the 184 social problems referred to the Almoners, 107 concerned patients with fractured femurs. Other fractures, especially those of the lower limb (apart from femur) were the most frequent sources of difficulties. The proportions of patients of each diagnosis receiving assistance are shown in Table IX. Often the illness of some other member of the family, or the inability to deal with minor nursing problems, necessitated a further stay away from home. As the patients were not ill enough to require hospital attention, and could not remain as in-patients occupying beds, a period of convalescence offered the ideal solution.

Specific cases illustrate the problems encountered:

1(*a*).—An old lady of 73 had a home to return to, but had no-one to attend to her; she could not go home until the necessary supervision was obtained. She was almost blind and had fallen at home, fracturing her pelvis and wrist; she lived in a 6-roomed house with lodgers, for whom there was a court order for eviction, and her relatives were hoping to use the lodgers' rooms. It was arranged that she should go home to live on the ground floor with a woman lodger who was at home all day, and her daughter visited daily and did the shopping.

1(*b*).—A widow of 84, living with her unmarried second son, fell at home and sustained a pertrochanteric facture of the femur. The patient was in hospital for 22 days and her injury was treated with a Neufeldt-Capener nail plate. She could not return to her own home, where her son was out all day. Her family of three sons and two daughters was disunited, both the daughters and the eldest son refusing to look after the patient, whom they described as very determined and difficult. The youngest son could not accommodate her unless absolutely necessary, because he was a prison warder, living next door to the prison, and felt these were not ideal surroundings for his mother; but ultimately, disgusted with the rest of the family, he took his mother to live with him, and his wife, who was a district nurse, managed with the aid of a home help.

1(*c*).—An old lady of 76 fell out of bed and fractured the upper shaft of her femur, for which she remained in hospital 173 days. About 3 months before this accident, a daughter-in-law had persuaded the patient to give up her home to go and live with her husband and herself, but now this daughter-in-law, who for health reasons could not do any lifting, did not want the patient back, and described her as "difficult". Another daughter-in-law also refused to have the patient, and they requested that a chronic bed should be applied for. When traction was removed, the leg refractured. Finally an infirmary bed was obtained and the patient was transferred.

Discussion

The findings of this survey support the belief of Sheldon (1948) in "the great importance in old people of the effects of falls and accidents, because of the severe injuries that may follow; in some cases a fall may precipitate a general break-up of the old person". In recent years the treatment and after care of the chronically ill elderly patient has been investigated (Thomson, 1949; Lowe and McKeown, 1949, 1950 a and b; Lowe (1950); McKeown and

TABLE IX

SOCIAL PROBLEMS AMONG ELDERLY IN-PATIENTS WITH DIFFERENT INJURIES (BIRMINGHAM ACCIDENT HOSPITAL)

Diagnosis	Social Problem										
	Dom. I	Dom. II	Infirmary	Convalescence	Home Help and District Nurse	Finance	Compensation	Home Nursing Equipment	Occupational Adjustment	In-patients only	All Patients
Head injury	1	4	—	1	—	—	—	1	1	8	45
Fractured pelvis, trunk etc.	4	4	1	—	1	2	—	—	—	12	39
Fractured upper limb	5	1	—	1	—	1	2	—	1	11	69
Fractured femur	36	38	5	6	10	4	1	6	1	107	203
Other lower limb fractures	7	8	—	2	3	3	—	1	1	25	85
Dislocation and strain	—	—	—	—	—	—	—	—	2	2	23
Laceration, contusion, superficial injury	2	2	2	1	—	—	—	—	—	7	86
Burn	2	3	—	—	—	—	—	—	—	5	21
Other accidents	2	1	—	—	—	—	—	—	1	4	9
Others	0	1	—	1	—	1	—	—	—	3	15
Total	59	62	8	12	14	11	3	8	7	184	604

Lowe (1950); Amulree and others, 1951; Graham, 1954), but little attention has been given to accidental injuries which incapacitate an elderly person, who may hitherto have been living a normal life.

It is not unduly surprising to find that domestic accidents are numerically more important than any other type, for elderly people spend much time at home. Of 2,909 domestic accidents studied by Castle (1950), 291 (10 per cent.) occurred in people over the age of 65. The difference in incidence between males and females is very striking, since 58 of the accidents happened to men and 233 to women. In contrast, the road accident lists in the United Kingdom (Ministry of Transport, 1954) show that 13,120 men and 10,666 women were injured. Of these, 850 men and 485 women died; the high number of fatal road accidents among men over 80, is confirmed by the records of Birmingham male in-patients. Industrial accidents have relatively little importance among people over 65, but although the rate of these accidents does not rise substantially with age, the severity and mortality increases (King and Speakman, 1953).

There are more women than men over 65 in the population, but this does not account for the excess of accidents. The approximate numbers of domestic accidents are 13 per 1,000 population for men and 43 for women, showing the greater susceptibility of females to this type of accident. Poor housing accommodation and overcrowding are responsible for many falls, but many are preventable; securing loose rugs to the floor, covering uneven floorboards, and wearing suitable shoes, would all help. The road accidents per 1,000 population remain almost steady at 2·3 for women, but for men they rise from 3·9 for the 60–79 year age group, to 4·4 for the 80+ age group. The fact that amongst men, mortality due to road accidents, after correction for population, is twice that for women, may be due to men being more often out of doors. Impaired sensory reactions, diminished agility, and physical frailty increase the tendency of these elderly people to fall; poor eyesight and hearing, and a slowed reaction time often warn them of danger when it is too late.

It is commonly assumed that the power of healing diminishes with advancing age. Studies such as those of Lecomte du Noüy (1916) tending to support this may not be relevant to common injuries. Lecomte du Noüy inferred that healing of epithelium across a skin defect was slower with increasing age, but, as Elman (1952) points out, after trauma, or operations following trauma, the common need is for a return of tensile strength between tissues. However, it is thought that impaired vascularity of tissues often retards or prevents normal healing, especially in the upper and lower extremities, and injuries in these parts do not heal so well in the aged as in the young. Fractures are the particular problem here, and in association with a deficient blood supply the bone becomes brittle and is more liable to break.

The present findings on the importance of fractures of the femur and the radius and ulna are in agreement with a recent symposium on fractures in the aged. The opinion was expressed that in patients over 70 years of age the fracture was of secondary importance compared with the complications arising from a long period in bed, and emphasis was placed on the necessity for early mobilization, to re-establish as full a function of the limb as possible, as well as the side-effects of a long stay in bed. For this reason, internal fixation was advocated as being an efficient method of relieving pain, provided the operation could be shown to be safe for the patient (Evans, 1953).

Infection is a particularly important complication of trauma and operations, since on the whole, the resistance of old people to infection is lower. This has now been to some extent offset by the introduction of chemotherapy as well as aseptic technique, but it still remains a major hazard.

For many old people recovery is uneventful, and with a sympathetic home background they have no difficulties on returning to their families. Others, in spite of the precautions taken, develop bed sores or pulmonary complications, or become irrational and incontinent, and require constant nursing after the original injury is healed. These patients' problems are rather social than medical. The family attitude varies widely: some have a strong sense of loyalty, and regardless of financial straits and poor home conditions, will do their utmost to look after the patient. Others are willing to take care of the patient, but find it impossible in practice. A few try to evade their responsibilities entirely.

SUMMARY

(1) A sample of 500 patients over 65 years of age admitted to an Accident Hospital has been studied.

(2) 849 in-patients discharged from Birmingham hospitals in 1952 after treatment for injuries have been analysed with respect to type of injury, duration of treatment, and mortality. Accident frequency related to population enabled comparisons of mortality to be made between England and Wales and Birmingham.

(3) More than half the accidents sustained by the elderly occur in their homes, women being more

susceptible than men. Falls are the commonest cause of injury.

(4) The incidence of road accidents reported in the United Kingdom and in Birmingham is higher for males than females. Two-thirds of the fatal road accidents among the elderly in the United Kingdom happened to men.

(5) Approximately 60 per cent. of the injuries requiring treatment in hospital were fractures.

(6) Patients with fractured femurs have the longest average duration of stay in hospital.

(7) 44 per cent. of all the accidental deaths were due to fractured femurs, though the highest case mortality for any one diagnosis was 33 per cent. for burns.

(8) About one-third of the elderly in-patients at the Accident Hospital had social problems on discharge, mostly concerning accommodation and home help.

I wish to thank Dr. J. P. Bull, whose interest and criticism have been invaluable, Mr. P. Lockhart, Head Almoner, and the records staff of the Birmingham Accident Hospital for help and cooperation. I am also indebted to Dr. K. Cross of the Birmingham Regional Hospital Board and to the records departments of Selly Oak Hospital and the United Birmingham Hospitals for providing details of Birmingham patients.

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SOME FEATURES OF LEUKAEMIA MORTALITY

BY

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During 1953 there were just over forty deaths per week from leukaemia in England and Wales. This was, of course, a small proportion of the total number of deaths, but the years of potential life lost by death from leukaemia were disproportionately great: greater, for example (reckoning life to the age of 75) than those lost by death from peptic ulcer, non-respiratory tuberculosis, or all diseases conventionally attributed to viruses. Leukaemia derives an added importance from the fact that its rate of increase in recent years has been greater than that of any other cause of death except lung cancer and coronary thrombosis. Yet hardly anything has been written about leukaemia from the epidemiological point of view.

There seem to be two reasons for this neglect: the number of cases observed by a single clinician is rarely sufficient to suggest any aetiological hypothesis; and a suspicion exists (also expressed in connexion with lung cancer and coronary thrombosis) that standards of diagnosis may have varied from time to time and from place to place in such a way as to vitiate any statistical analysis. The present study therefore suffers from two faults: that it had to be based entirely on secondary sources, and that it had to be conducted as if diagnostic standards were always uniform. This may not deprive the conclusions of all value; for example, the effect of regional variation in speed of diagnosis is kept to a minimum by restricting attention to death certificates.

Type, Sex, and Age Distribution of Leukaemia Deaths

Since the introduction of the Sixth Revision of the "International Classification of Diseases and Causes of Death" (in which leukaemia has been transferred from "Diseases of the Blood and Blood-forming Organs" to "Malignant Neoplasms"), the national statistics of the United Kingdom have distinguished three types of leukaemia:

(*a*) Myeloid (45 per cent. of all leukaemia deaths, 1950–53);

(*b*) Lymphatic (37 per cent.);

(*c*) Monocytic (9 per cent.).

No distinction is made between acute and chronic forms of the disease, but deaths which have not been classified as belonging to any of the three main groups are described either as "acute leukaemia of unspecified type" (6 per cent.) or as "other and unspecified leukaemia" (3 per cent.).

There is a slight excess of males among persons dying of leukaemia. This is principally due to the high sex ratio $\left(\frac{M}{F} \times 100\right)$ in the lymphatic type. Sex ratios in the years 1950–53 were:

Lymphatic leukaemia ..	58	per cent. male
Monocytic leukaemia ..	54	
All types of leukaemia ..	53	
All causes of death ..	51	
Myeloid leukaemia ..	49	

The contrast between the two main groups is much too large to be attributed to chance (χ^2 with one degree of freedom, 59·01; $P < 10^{-10}$). Moreover it has not resulted from the greater proportion of females at risk in the elderly population, since this would have tended to lower the sex ratio for lymphatic leukaemia in relation to that for the myeloid type (see below). Nor can this result be attributed to variations in diagnosis. There is therefore some aetiological difference between the two main types of leukaemia, which must be associated with a difference between the sexes in exposure or susceptibility to leukaemogenic influences.

The relationship between age and leukaemia mortality is shown in Fig. 1, which indicates that, though the death rate is rather high among children, the heaviest mortality during 1950–53 was experienced by men and women between the ages of 65 and 80.

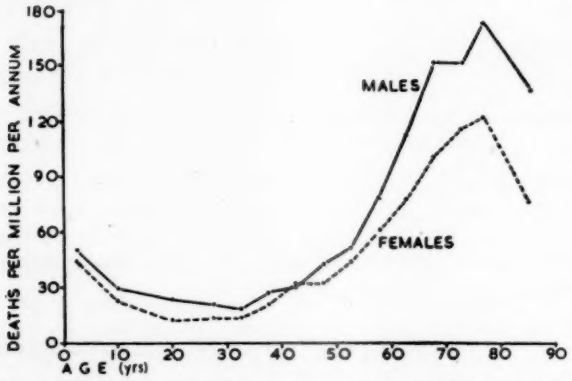

FIG. 1.—Mortality from leukaemia, by sex and age, England and Wales 1950–53.

The apparent tendency for risk of death from leukaemia to decline after the age of 80 may be merely a transient feature of the age-specific mortality curve. This is shown by Fig. 2 which presents a longitudinal or "cohort" view of the mortality experienced by groups of persons born in different decades. Members of the 1871 cohort were subject to a much greater risk of death from leukaemia during their early eighties than at any previous period of their lives. Later "cohorts" have also experienced a much more rapid increase during adult life in the risk of death from leukaemia than is suggested by the cross-sectional view shown in Fig. 1. Thus the age-curve for death from leukaemia seems likely to take on a shape something like that regarded by Nordling (1953) as typical of malignant diseases.

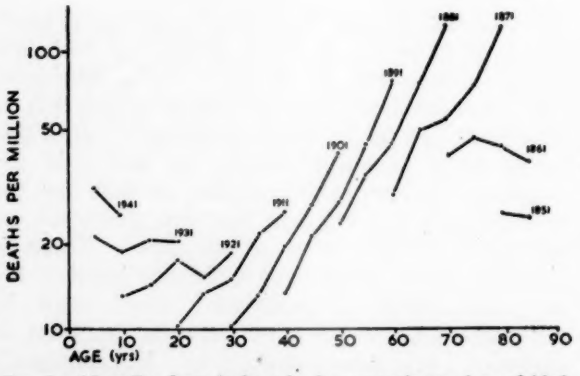

FIG. 2.—Mortality from leukaemia, by approximate date of birth, log. scale, sexes combined.

Different age groups show wide contrasts in the proportion of deaths ascribed to each type of leukaemia (Fig. 3). Among young children the lymphatic type is nearly twice as common as the myeloid type. By the age of 30 these proportions are reversed, but lymphatic leukaemia appears to increase in relative importance during the forties and fifties, and again becomes the commonest type at ages over 70. This relationship between age and the ratio of lymphatic to myeloid incidence is of interest because comparisons will be made below between populations in which no distinction as to type of leukaemia is possible. There is a slight presumption that when a population has an excess of leukaemia in the central age groups this may be associated with a relatively heavy mortality from the myeloid type. Conversely, if a population is found to suffer an excess of leukaemia which increases with age, then this may be associated with a heavy mortality from the lymphatic type.

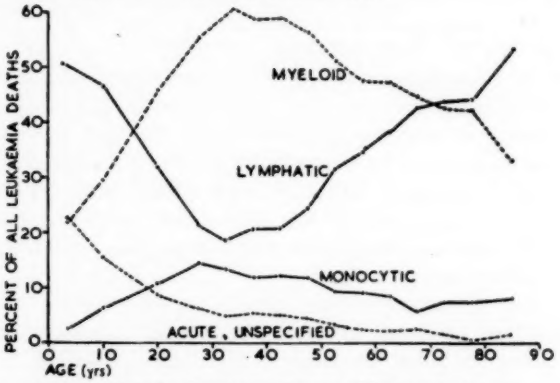

FIG. 3.—Relative frequency of types of leukaemia, by age.

Fig. 3 also shows that the "acute unspecified" type is commonest, as would be expected, at the youngest ages, and that it declines in relative importance throughout life.

LEUKAEMIA MORTALITY IN CHILDREN UNDER FIVE YEARS OF AGE

The peak of mortality in the under-5 age group, unlike the later peak, seems to be a permanent feature of leukaemia. It is possible to locate this early peak more accurately by using the numbers of deaths and population at risk which are available for individual years of life from 0 to 5. These figures reveal a marked discontinuity in the risk of death from leukaemia during early childhood (Fig. 4, opposite).

In the first few months of life the death rate was between 25 and 30 per million and in the second year of life only a little higher. But in the third year it rose to twice its original level with a further small

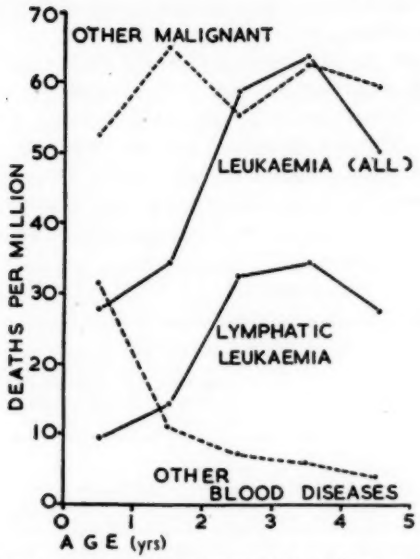

FIG. 4.—Mortality from leukaemia in children under 5 years of age, 1950–53.

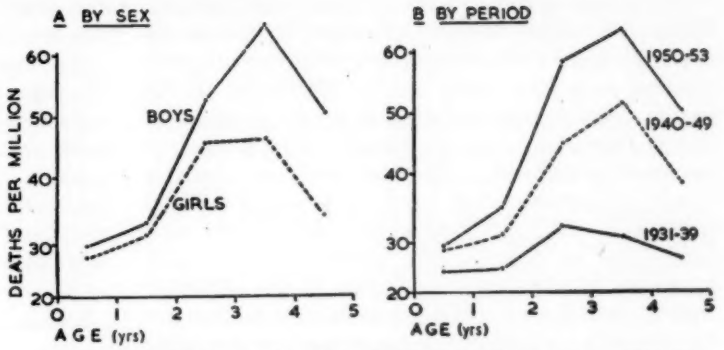

FIG. 5.—Mortality from leukaemia in children under 5 years of age, 1931–53.

rise in the fourth year. The death rate from *lymphatic* leukaemia among 2-year-olds was more than three times as great as among infants of 0 to 12 months. This abrupt, upward change in mortality has no parallel in any other cause of death for which statistics are available*. It is quite different from the age-gradient for other malignant diseases and for non-neoplastic diseases of the blood and blood-forming organs. This phenomenon appears to affect boys more than girls, and to have become more important during recent years (Figs 5A and 5B).

Statistics of deaths in the U.S.A. show that a rise in mortality between the second and third years of life has been a feature of leukaemia in that country also, at least since the "cohort" of 1931. Moreover this rise seems to have been greater for the first post-war babies (Table I).

TABLE I

U.S.A. LEUKAEMIA DEATHS IN ONE-YEAR-OLD BABIES AND IN TWO-YEAR-OLD BABIES DURING THE FOLLOWING CALENDAR YEAR, BY APPROXIMATE YEAR OF BIRTH

Yr of Birth	Deaths		Percentage Excess of 2-yr-olds
	1-yr-olds	2-yr-olds	
1931–33	161	216	34
1933–36	185	252	36
1937–39	256	326	27
1940–42	274	378	38
1943–45	331	429	30
1946–48	348	612	76

* The incidence of tuberculous meningitis increases between the first and second years. American figures suggest that cancers of the brain and of the kidney are commoner in the second than in the first year of life.

At least two American groups—Bufkin and Davison (1943) and Cooke (1942)—have had under review sufficient hospital cases of leukaemia to show that a peak occurs in the third and fourth years of life.

Cooke asserts that the age-incidence curve of leukaemia in childhood follows that of the acute childhood infections which she considers to be important factors in the causation of leukaemia. As far as *fatal* cases of childhood exanthemata are concerned this is certainly not true, but the age-curve for leukaemia may conceivably follow the age-incidence curve of non-fatal cases. However, Cooke's hypothesis would in any case not explain the recent accentuation of the leukaemia peak in childhood.

Regional Variation within England and Wales

Death from individual causes in the different regions of England and Wales are published only for a selected list of diseases, which did not include leukaemia until 1950. Consequently, only 4 years' records of leukaemia deaths (numbering 7,923) are available for analysing regional variations in mortality.

The method of analysis used here is identical with that used by the Registrar-General in his studies of occupational mortality. Age-specific death-rates for the country as a whole have been applied to the numbers of persons of various ages in each local population to obtain a "standard" number of deaths.

When divided into the number of deaths in any area, this provides a mortality ratio, conventionally expressed as a percentage. For the present purpose nine age groups have been used for each sex so that the standard number of deaths for a region is the sum of eighteen separately-calculated expectations.

The results of this analysis are shown in Table II. There is a fairly regular gradient in leukaemia mortality from a relatively low level in the north of England to a level about half as high again in the south. That is, the variation is about as great as (but in a generally *contrary* direction to) the regional variation in stillbirths and neonatal deaths, both of which are considered to be fairly sensitive to local conditions. This north-to-south gradient may owe something to the varying proportions of each economic class which are found in the different regions, but the regional differences in leukaemia are too large to be regarded as secondary to economic differences. The same general gradient can be observed in mortality ratios calculated for the sexes separately.

TABLE II

LEUKAEMIA MORTALITY IN THE STANDARD REGIONS OF ENGLAND AND WALES
STANDARDIZED FOR AGE AND SEX, 1950–53

Region	No. of Deaths		Mortality Ratio
	Actual	Standardized	
Southern (Berks, Bucks, Dorset, Oxford, Hants, I.O.W.) ..	601	496·15	121
South Eastern (Parts of Essex, Kent, Herts, Middlesex, Surrey, Sussex)	570	501·32	114
Greater London	1,685	1,483·29	114
Midland (Hereford, Salop, Staffs, Warwick, Worcs) ..	768	763·84	101
Eastern (Beds, Cambs, Ely, Part of Essex, Part of Herts, Hunts, Norfolk, Suffolk) ..	554	580·34	95
South Western (Cornwall, Devon, Glouc, Somerset, Wilts)	543	569·03	95
North Midlands (Part of Derbyshire, Leics, Lincs, Northants, Notts, Peterboro', Rutland)	569	606·25	94
Yorkshire (East and West Ridings)	683	735·93	93
North Western (Cheshire, Lancs, Part of Derbyshire)..	1,069	1,162·01	92
Wales	421	471·12	89
Northern (Cumb, Northumb, Durham, Westmor, North Riding of Yorks)	460	553·69	83

None of the great cities of England and Wales, apart from London, had an exceptionally high or low leukaemia death rate during 1950–52.* In particular the nine County Boroughs in which there are teaching hospitals registered 618 deaths compared with a standard number of 606. One would hardly have expected such a close agreement between registered and standard deaths in these boroughs if local variations in diagnostic standards had had any important effect on the reported death rate from leukaemia.

So slight are the differences between the county boroughs that regional variation can be shown to arise chiefly from variations in rates *outside* the main towns. The ten standard regions other than London have been grouped in two sets of five (on the basis of their mortality ratios), and the registered and standard deaths have been aggregated for each set (Table III).

TABLE III

Regions	Mortality Ratio	
	Aggregate of County Boroughs	Aggregate of Administrative Counties
Five with high mortality ratios	100·7	107·8
Five with low mortality ratios	96·4	84·4
Difference..	4·3	23·4

For leukaemia, a simple comparison between urban and rural areas cannot be made, for in the north of England urban mortality tends to exceed rural mortality, while in the south the reverse is the case. Even this is an over-simplification, as is shown by subdivision of the largest region in the south. Within Greater London the central L.C.C. area (which has the greater affinity to county boroughs in other parts of the country) had a higher mortality than the outer ring (120 compared with 110). The L.C.C. area is, however, by no means homogeneous. Four contiguous Metropolitan Boroughs in the north-west (Chelsea, Westminster, St. Marylebone and Hampstead) had together a mortality ratio of 185, while four others on the south side of the river (Southwark, Bermondsey, Lambeth, and Camberwell) registered only 93 per cent. of their standard deaths.

The excess of leukaemia deaths in the L.C.C. area as a whole was almost identical for the two sexes (male mortality ratio, 113; female, 114) but the excess increased with age:

Age (yrs)	*Mortality Ratio*
0–4	93
5–24	102
25–44	105
45–64	119
65–74	121
75+	203

This tendency for regional variation to be greatest in the oldest age groups can also be demonstrated in areas outside London.

* For county boroughs and for subdivisions of greater London the only figures which give the age-distribution of the populations at risk are those from the 1951 Census. A separate analysis had therefore to be made for the three years immediately surrounding the census date, this time using only eight age groups in each sex.

Comparison of England and Wales with Other Countries

The method of comparison applied to the regions of England and Wales can be extended to other countries which publish statistics of deaths from leukaemia, provided that there is also available a contemporary estimate of the populations at risk in a number of age groups (Table IV). The sources of the statistics used are given with other references at the end of the paper. In each case the comparison is based on the age-specific death rates current in England and Wales during the years for which the other country's figures were available. The number of age groups used in the standardization was in every case greater than the number for which separate mortality ratios are shown in Table IV).

Scotland.—The number of deaths from leukaemia registered during 1950–52 was 635. This is very close to the 659 deaths which would have been expected on the basis of the age-specific rates for England and Wales. The ratio of myeloid to lymphatic cases was, however, higher than in England and Wales. This observation may be related to the apparent tendency for the Scottish death rate to be relatively high during the middle part of life, when the proportion of myeloid cases is highest (Fig. 3). As in England and Wales, lymphatic leukaemia in Scotland showed a greater excess of males than other types:

Lymphatic leukaemia ..	58	per cent. male
All forms of leukaemia ..	52	
Myeloid leukaemia ..	47	

Northern Ireland.—Deaths attributed to leukaemia were significantly less common during 1950–52 than in England and Wales as a whole. This difference was most conspicuous among the older age groups who suffered only about a half of their "standard" deaths. Between the ages of 35 and 54, on the other hand, there was a clear excess of leukaemia deaths in Northern Ireland. This may mean an occupational risk somewhere in the six counties, partly because of the age group involved, but chiefly because the entire excess occurred among men. These "extra" deaths cannot be located precisely from the published statistics for localities of Northern Ireland, since these figures do not separate leukaemia from Hodgkin's disease.

Eire.—The mortality ratio is even lower than for the northern part of the island, and again the greatest deficit in "expected" deaths was in the oldest age group.

U.S.A.—During 1949–50 leukaemia mortality was much higher than in England and Wales; the high total resulted from the large number of deaths attributed to leukaemia among the white population. Whereas young men and women on each side of the Atlantic appear to be about equally liable to die of leukaemia, the rates for individuals who were past working age were two or three times higher in America than in England. This suggests the possibility of a difference in diagnostic standards, at least in elderly patients. But the differences between the two countries for neoplasms of some other sites, where the diagnosis is rarely in doubt, are equally great. A national difference in diagnostic practice could not explain both comparisons in Table IV, since non-white Americans had, generally, speaking, much lower death rates from leukaemia than the English. Despite the very low rates for non-whites at each extreme of life, the mortality ratio for coloured persons in the age group 35–44 was even higher than that for white Americans. A closely parallel finding for cancer of the lung has been reported by Hoffman and Gilliam (1954), who comment:

> This age differential in rates does not appear to be consistent with the view that the lower total mortality for the non-white population is due to inadequate diagnostic facilities.

Mortality differences between the white and coloured population of the United States are variously interpreted as being due to racial, social, or geographical factors. There is little evidence that racial or genetic factors are important in human leukaemia, however, and no study of the geographical distribution of the disease within the United States is yet available. It therefore seems reasonable to regard the relatively low rates among non-whites as evidence of the influence of social conditions (see below).

Table IV

LEUKAEMIA MORTALITY IN CERTAIN COUNTRIES, EXPRESSED AS PERCENTAGE OF CONTEMPORARY MORTALITY IN ENGLAND AND WALES, STANDARDIZED FOR AGE AND SEX

Country	Period	All Ages Combined			Sexes Combined, by Age Group													
		Persons	Males	Females	0–	5–	10–	15–	20–	25–	30–	35–	40–	45–	50–	55–	60–	65–	70–	75–
Scotland ..	1950–52	96	94	98	92	97				104				102		86		99		91
Northern Ireland	1950–52	86	86	85		95		90				140					55			
Eire	1950	64	65	63		84			71						61			48		
U.S.A. White	1949–50	153	153	152	129	129		94		109		136		143		151		195		306
U.S.A. Non-white	1949–50	83	85	80	57	64		70		85		140		102		109		63		56
Germany ..	1948	88	90	85	74	88		107			94			99			89		56	
Denmark ..	1951–52	147	151	141	121	96			122						137			200		219

Germany.—Although the Federal Republic had, during 1948, a death rate from leukaemia which was appreciably lower than the contemporary rate in England and Wales, persons of working age were as liable to die of leukaemia in Germany as in Britain. The difference between the countries was due to the relatively low rates for the very young and very old in Germany; the oldest age groups showed the greatest contrast.

Denmark.—Here the population is considerably smaller than that of Scotland, yet had as many deaths from leukaemia in 2 years as did Scotland in 3 years. This country provides the most challenging example so far revealed of a geographical differential in leukaemia. In environmental and social conditions Denmark must more closely resemble Britain than it does the United States. Yet in Denmark leukaemia mortality is approximately equal to that in the United States. The payment of a notification fee for cases of leukaemia may stimulate Danish physicians to make the diagnosis in cases where it would have been overlooked by a British doctor, but this seems unlikely to provide the full explanation.

Social and Occupational Incidence of Leukaemia

The last full occupational mortality analysis (Registrar-General, 1938), now more than 20 years out of date, includes leukaemia together with Hodgkin's disease under "Leukaemia, etc.".

Social Class.—This group of diseases occurred in excess at the upper end of the economic scale, particularly among older persons. For males of all ages over 16 the Social Class mortality ratios were as follows:*

Social Class	*Ratio*
I Professional and administrative	176
II Intermediate	125
III Skilled manual workers ..	96
IV Intermediate	93
V Unskilled workers	84

Grouping together Social Classes "I and II" and "IV and V" gives the following ratios:

Age	*I and II*	*IV and V*
16–34	1·52	1
35–64	1·41	1
65 and over ..	2·05	1

The social gradient for married women was as great as that for men.

Occupation.—None of the individual occupations distinguished in the Registrar-General's analysis had a significant excess of death from "leukaemia, etc.", but employers and managers as a whole (all in Social Class II) had a mortality ratio as high as that of Social Class I. It is not easy to believe that an occupational factor could explain the high rate among employers and managers; this and the general social gradient are more likely to have resulted from some factor common to all well-paid persons at that time (1930–32). An abbreviated analysis of mortality in the different economic strata of England and Wales has been prepared (Registrar-General, 1954) from the deaths registered during 1950 together with the ONE per cent. sample of the 1951 census records. This agrees with the previous analysis in indicating a social distribution of leukaemia which is:

(*i*) unfavourabe to the higher income groups,
(*ii*) more uneven at ages over 65 than during working life.

An economic gradient in leukaemia has been reported from the U.S.A. by Sacks and Seeman (1947), where the excess again occurs at the upper end of the economic scale. In the United States also an occupational risk has been established by March (1950), who estimates that radiologists have a death rate from leukaemia nine times as high as that for other physicians. This implies a very high risk indeed, as the control group used—physicians other than radiologists—are thought by Peller and Pick (1952) to have a death rate from leukaemia about three times as high as that for the general white population.

Trend and Possible Short-Term Changes in Leukaemia Mortality

As measured by the Comparative Mortality Index (which allows for changes in the age-composition of the population) leukaemia mortality in England and Wales was more than 2½ times as heavy in 1953 as it had been in 1931. In each sex the course of this Index has been close to an exponential curve, correlation coefficients between the logarithm of the index and time being +0·99 and +0·98 for males and females respectively. The rates of increase over this period, estimated from fitted curves, were 4·3 per cent. per annum for males, and 4·0 per cent. per annum for females.

Despite the close fit of the annual points to the logarithmic trend, there were significant differences between the actual and "expected" numbers of deaths.* The outstanding years were 1941 and 1948, in each of which about 10 per cent. of the "expected" deaths failed to occur. In 1941 the

* The ratios published by the Registrar-General are for the restricted age group 16–64.

* For the whole period, sexes combined, χ^2 with 21 degrees of freedom = 39·88, $P < 0·01$.

deviation from trend applied equally to males and females. In 1948 the deficiency was largely in deaths of females, but an equivalent deficiency of male deaths occurred in the *two* years 1947–48.

A feature of the rise in leukaemia mortality which has been commented on both by the Registrar-General and by American observers is the disproportionately large rise in the age-specific death rates at ages over 65. There are many possible interpretations of this phenomenon with, as yet, little to choose between them. It does *not* necessarily imply any disproportionate exposure of elderly persons to leukaemogenic influences, since the latent period for malignant disease may be 20 years or more.

Leukaemia mortality seems to be little affected by the seasons of the year. Over the 6 years 1948–53 (covering 11,000 deaths), after making due allowance for trend and for differences in the length of months, it was found that the months of highest apparent mortality were June and July, and the lowest April and May. But the range of the apparent fluctuation was not statistically significant. In this lack of seasonal movement leukaemia differs from most diseases, including other malignant neoplasms.

It seems likely, however, that short term fluctuations of a non-seasonal character do occur, at least in the numbers of male deaths. An examination of fluctuations in the numbers of leukaemia deaths during the 21 quarters up to the end of 1953, after adjustment for trend and for differences in the number of days per quarter,* showed that significant deviations had occurred in male deaths, but not in female deaths.† On three occasions in the figures for males a high quarterly mortality was followed immediately by a low mortality.

In view of the hypothesis that an acute infection may influence the development of leukaemia, a search was made for fluctuation in relation to the one major epidemic affecting adults in recent years, namely the influenza outbreak early in 1951. Unfortunately the hypothesis gives no guidance regarding the time-lag to be expected. It is also possible that a temporary influence shows its effect, if any, after different intervals for men and for women (a point discussed above). Since the heaviest influenza mortality and sickness benefit claims during this epidemic occurred in the North-West Region of England (Massey and Logan, 1951), Table V is of interest.

TABLE V

LEUKAEMIA DEATHS IN NORTH WEST REGION OF ENGLAND

Year	Males	Females
1950	128	123
1951	120	128
1952	168	118
1953	131	153

Comparison of the 1952 deaths for males and the 1953 deaths for females with those of the preceding years suggests that leukaemia mortality in this region had been disturbed. A statistical test confirms that there was a significant variation in the sex ratio of leukaemia deaths in this region during the years 1950–53.*

DISCUSSION

It is well known that by intensive inbreeding strains of mice can be produced which differ sharply in their liability to develop leukaemia. The very rapid increase of this disease in man within the last generation cannot, however, be attributed to genetic influences. We are therefore obliged to look for some new factor (or factors) in the environment, which has been operating for 25 years at least, and possibly since the 1860s. Men and women appear in general to be equally exposed to this influence, so that the overall increase in mortality is unlikely to be related to such variables as occupation, smoking, or cosmetics. A dietary habit, such as the consumption of a preserved, dyed, or synthetic food, would provide a more plausible hypothesis for investigation, particularly as some dyestuffs are known to be capable of causing malignant change in human cells. Sulphonamides and the newer antibiotics, which some doctors have regarded as possible agents, have not been available long enough to be held responsible for the rising mortality, for the trend of leukaemia has shown no important change since 1931 (and possibly earlier). On the other hand the use of *X* rays goes back to the beginning of the century. *X* rays are known to act as a leukaemogen or co-leukomogen on laboratory animals, and are thought to be responsible for the one established example of occupational risk of leukaemia. Gamma radiation has also been incriminated as a cause of

* As population estimates are not available for each quarter, the trend had to be fitted to the absolute numbers of deaths. Deaths of service-men and women have not always been included in the published tables of deaths in each month. Demobilization might therefore have affected the quarterly figures, and for this reason the analysis was not carried back further than the end of 1948.

† χ^2 with 19 degrees of freedom = 40·46, $P < ·017$ males; 15·18, $P > ·707$ females.

* χ^2 with three degrees of freedom = 10·81, $P < ·02$.

leukaemia in survivors from the atomic explosions in Japan (Folley, Borges, and Yamawaki, 1952).

The influence should also be one to which residents in the south and south-east of England have been more exposed than those in the north and north-west. It must affect the rich more than the poor, but must by now be widely diffused through society, for the mortality contrast between the most widely separated social groups is less than that between the 1931 and 1953 rates for the community as a whole. The geographical variation within England may have a common source with the social variation, since the areas most affected are those in which the standard of living is highest. But variation in living standards cannot explain all the geographical variations in leukaemia. For example, the gross excess of leukaemia in Denmark by comparison with neighbouring Germany must be attributed to something more specific than the general standard of living. It is not impossible that the higher rate in Denmark may have arisen from an exceptionally wide use of radiography and radiotherapy.

Summary

The incidence of deaths attributed to leukaemia is shown to have varied greatly:

(*a*) As between years (1953 more than 2½ times as high as 1931);

(*b*) As between different countries (U.S.A. and Denmark > England, Wales and Scotland > Western Germany > Ireland);

(*c*) As between different regions of England (south > north);

(*d*) As between economic strata (rich > poor);

(*e*) As between races in the U.S.A. (white > non-white).

In all five of these contrasts the sexes have been affected to an approximately equal extent and the oldest age group has been affected more than any other.

Four anomalous findings are the following:

(*i*) there is an abrupt increase in the risk of death from leukaemia between the ages of one and two;

(*ii*) the regional variation within England hardly affects the leukaemia mortality of the County Boroughs;

(*iii*) the otherwise steady rise in the Comparative Mortality Index appears to have been interrupted in 1941 and again in 1947–48;

(*iv*) the numbers of male deaths from leukaemia per quarter in recent years show non-random fluctuations which do not appear to be either secular or seasonal.

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FERTILITY AND REPRODUCTIVE HISTORY OF MOTHERS OF MONGOLOID DEFECTIVES

BY

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In a previous communication (Smith and Record, 1955) it was observed that there appeared to be an association between mongolism and primogeniture which invites investigation of the fertility of mothers of mongols. Such a study is by no means new. It has been attempted by many previous workers, prompted perhaps by the observations that the risk of producing a mongol increases sharply with advancing maternal age and that fertility of women becomes impaired as age increases.

Various indices of fertility have been used. The one most easily recorded is the size of the family at the end of the reproductive period. Shuttleworth (1909) considered that families containing a mongol tended to be larger than usual, but Brousseau (1928) regarded family size as unimportant; in neither case was comparison with a control group attempted. Penrose (1949), using fraternities containing non-mongoloid mental defectives as controls, found that mean sibship size was raised in families containing mongols. This observation could easily result from the higher maternal age at which mongols are born; by controlling this variable, Jenkins (1933) showed that the mongols of Shuttleworth's and Brousseau's series came from families rather smaller than average. The matter cannot be regarded as settled, however, since the control group used by Jenkins (U.S. births in 1927) probably differed considerably from the population from which the cases were drawn. A further objection is that the cases were diagnosed some time after birth; the increased risk of infection to which members of large fraternities are exposed, and the high mortality of mongols from infectious disease, would tend to eliminate at an early age mongols born into large families.

Another measure of fertility is the pregnancy-free interval preceding birth. The view that this interval was longer than usual was first recorded by Langdon Down (1909). Although no comparison with a control group was attempted, Beidleman (1945), Benda (1946, 1949), and Engler (1949) supported this view, but Penrose (1934) and Bleyer (1938) considered it to be unimportant. The effect of maternal age appears to have been ignored except by Jenkins (1933), who found that the mean pregnancy-free interval preceding mongol births was longer than that shown by the general population of comparable age. This result, however, cannot be unreservedly accepted in view of the unrepresentativeness of his control group.

The pregnancy-free interval before mongol births has also been compared with the interval before the birth of unaffected sibs. By this technique, Øster (1953) showed that the period preceding the mongol conception appeared to be longer. The method presents many difficulties, one of which (referred to by Record and McKeown, 1950) arises from the fact that the larger, and therefore more fertile, families are unduly represented among the normal sibs. Øster avoided this error by restricting comparison to the same birth-rank intervals, but was consequently prevented from matching for maternal age, since in each fraternity he chose unaffected sibs born before the mongol. Two sources of error were thus introduced:

(*a*) in general, mothers would be older, and therefore less fertile, at the birth of the mongols than at the birth of the sibs;

(*b*) since sibs and mongols were matched for birth rank, sibs would be drawn from larger families than the mongols with whom they were compared.

Fertility after a mongol birth has received little attention. Øster (1953) reported that the interval between the birth of a mongol and the next conception was longer than that which followed births of succeeding unaffected sibs. Since he compared mongols with sibs of the same birth rank, he was comparing mothers who may have had no more than

one child after the mongol with those who had had at least two. Control of birth rank may make this comparison acceptable provided fraternities are complete when the data are recorded. Since part of Øster's series did not satisfy this condition, his comparison was made against a group weighted in favour of the more fertile mothers, and his result may therefore not be free from bias.

We have been unable to find in the literature any reference to fertility studies based on a comparison of mothers of mongols with a representative control group of mothers of similar age. Inaccurate results are likely if affected and controls are derived from different populations, and failure to take account of differences in maternal age is certain to be misleading. Attempts to analyse the data by comparison with unaffected sibs are equally unsatisfactory. Error may also arise if the diagnosis of mongolism is delayed until some time after birth, since the mortality of mongols from infection in infancy is high and is almost certainly related to family size.

It seemed worth while to investigate this problem by comparing a series of mongols, most of whom were diagnosed soon after birth, with a selected control group.

Material

The mongol series, consisting of 252 cases born in the years 1942–52 to mothers normally resident in Birmingham, was assembled as previously described (Record and Smith, 1955). Details of the mothers' reproductive histories were obtained by interview and are complete for 217 cases. Comparable data were not available from the original source for the control group (consisting of 1,156 births representative of all births in the city in the same period) used in the maternal age and birth rank analysis (Smith and Record, 1955), and the information required could be obtained only by interviewing mothers. The amount of field work was reduced by selecting a sample of the control group. An attempt was made to match control births according to maternal age with the 252 mongols. This attempt was not completely successful and the control sample thus selected consisted of only 216 births, of which 139 were traced and the mothers interviewed. The field work on both mongol and control groups was carried on concurrently by the same investigators. The more efficient tracing of the mothers of mongols can probably be explained by the fact that many were known to the Local Authority's Mental Deficiency Section which was able to provide up-to-date addresses, whereas the only addresses available for controls were those given at the time of birth.

Results

Before attempting a detailed analysis of the data, it is necessary to determine whether the mongol and control series are comparable in respect of variables which may be expected to influence fertility. Table I shows the two series distributed according to maternal age at birth of propositi. Some discrepancy is revealed, particularly at the age group "40 and over" where the control group is deficient. This is because births at these ages are relatively infrequent and there were not enough in the original control group to permit exact matching. It is clear that maternal age cannot be disregarded in the following analysis.

TABLE I

DISTRIBUTION OF MONGOL AND CONTROL PROPOSITI ACCORDING TO MATERNAL AGE

Maternal Age (yrs)	Mongols		Controls	
	No.	Per cent.	No.	Per cent.
Under 25 ..	14	6·5	14	10·1
25–	36	16·6	21	15·1
30–	40	18·4	29	20·9
35–	59	27·2	39	28·1
40 and over ..	68	31·3	36	25·9
Total ..	217	100	139	100

Another variable which obviously influences fertility is age at marriage (Table II). A crude comparison shows that mothers of mongols married slightly later than control mothers. Since women having children relatively late in life married, in general, later than younger mothers, this result could be due to the fact that the mongol and control propositi are not exactly matched in respect of maternal age. Support for this explanation is provided by standardizing the two series in order to remove the effect of variation due to maternal age at birth of propositi; the difference between the means is almost eliminated by this technique.

TABLE II

AGE AT MARRIAGE

Age at Marriage (yrs)	Mothers of Mongols		Mothers of Controls	
	No.	Per cent.	No.	Per cent.
Under 20	33	15·5	22	16·2
20–	88	41·3	63	46·3
25–	56	26·3	35	25·7
30–	21	9·9	12	8·8
35 and over	15	7·0	4	2·9
Total	213	100	136	100
Mean Age (Crude) ..	24·54		23·82	
Difference	0·72 ± 0·54			
Mean Age (Standardized)*	24·34		24·13	
Difference	0·22			

Four mothers of mongols and two control mothers were unmarried. Age at marriage was not recorded for one control mother.

* The mongol and control series are standardized to the same distribution of maternal age at birth of propositi.

FERTILITY BEFORE BIRTH OF A MONGOL.—An index of the mother's fertility during the period between marriage and the conception resulting in the propositus is derived from the number of pregnancies occurring within the period. This value is partly dependent on age at marriage and partly on duration of marriage. It has been shown (Table II) that variation arising from differences in age at marriage can be removed by standardizing the affected and control groups to the same distribution by maternal age at birth of propositi. This procedure also removes the effect of differences between the two groups in duration of marriage, since if both age at marriage and age at birth of propositi are fixed, the two groups must be comparable in respect of duration of marriage. (We satisfied ourselves that this was so by calculating the mean duration of marriage for the two standardized series; values of 10·40 and 10·75 years were obtained for mothers of mongols and controls respectively.)

Restricting attention to pregnancies which proceed to a viable stage (at least 28 weeks), we note (Table III) that in general, the birth of a mongol is preceded by fewer pregnancies than that of the control propositi of comparable maternal age (standardized means are 2·07 and 2·31 respectively). This result is, of course, consistent with the primogeniture effect previously observed (Smith and Record, 1955). Since mothers of mongols and of controls are comparable in respect of age at marriage, it seems likely that the relatively increased incidence of mongolism among first born is due to impairment of fertility at some time before the mongol conception. It should be noted, however, that fertility has here been interpreted in a demographic sense, pregnancies failing to reach a viable stage being ignored. It has often been asserted that mothers of mongols experience a higher abortion rate than other women; the present series provides support for this view, the incidence of abortions in pregnancies preceding births of mongol and control propositi being 10·1 and 7·2 per cent. respectively. After correction for differences in maternal age, the abortion rates of the two series were 10·3 and 6·7 per cent. When abortions are added to viable pregnancies and the two series standardized as before, the mean numbers of prior pregnancies are 2·31 and 2·49 respectively for mothers of mongols and controls (difference $0·18 \pm 0·27$).

It is concluded that examination of the period between marriage and a conception resulting in a mongol provides little evidence of impaired fertility. It is possible of course that a more detailed examination may reveal differences between the two groups. For example, there may be an initial period of high fertility followed by one of impaired fertility terminating with the mongol conception. In order to examine this point, pregnancy-free intervals before propositi and before their prior sibs have been calculated. The periods were measured from the termination of one pregnancy to the conception of the next. In the case of first pregnancies, the interval was measured from the time of marriage, pre-marital conceptions being exluded.

Examination of pregnancy-free intervals immediately preceding conceptions of propositi is based on 208 mothers of mongols and 137 controls (Table IV).

TABLE IV

MEAN PREGNANCY-FREE INTERVALS (MONTHS) IMMEDIATELY PRECEDING CONCEPTION OF PROPOSITI

Maternal Age (yrs) at Birth of Propositus	Under 25	25–	30–	35–	40 and over	All Ages
Mothers of Mongols	11·6 (9)	28·5 (35)	54·2 (39)	65·9 (58)	79·0 (67)	58·0* (208)
Mothers of Controls	13·2 (13)	47·6 (21)	52·6 (28)	53·0 (39)	65·2 (36)	53·2* (137)

Numbers of mothers are given in brackets.
Nine mongols and two control propositi resulting from pre-marital conceptions have been excluded.
* Standardized to the maternal age distribution of the combined series.

TABLE III

PREGNANCIES PRECEDING CONCEPTION OF PROPOSITI

Maternal Age (yrs) at Birth of Propositus	Under 25		25–		30–		35–		40 and over		All Ages	
	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls
No. of Mothers	14	14	36	21	40	29	59	39	68	36	217	139
No. of Preceding Viable Pregnancies	3	2	37	10	47	46	139	112	236	139	462	309
Mean No. of Preceding Viable Pregnancies	0·21	0·14	1·03	0·48	1·17	1·59	2·36	2·87	3·47	3·86	2·07*	2·31*
No. of Preceding Abortions	0	2	4	0	10	4	16	10	22	8	52	24
Mean No. of All Preceding Pregnancies	0·21	0·29	1·14	0·48	1·42	1·72	2·63	3·13	3·79	4·08	2·31*	2·49*

* Standardized to the maternal age distribution of the combined series

Standardization of the means to the same maternal age distribution gives values of 58·0 and 53·2 (difference 4·8 ± 4·9 months). In this analysis, abortions have been ignored and fallow periods have been calculated from the termination of the preceding viable pregnancy. If abortions are recognized and the term "pregnancy-free interval" interpreted strictly, the means are reduced (53·8 and 49·3 months), but the difference (4·5 is not much affected. We conclude that if, as has frequently been asserted, mongols are conceived after a period of infertility, a much larger series than the present one would be required to establish the point.

We now consider fallow periods preceding pregnancies which occurred before that which resulted in a propositus; the number of pregnancies for consideration in each sibship varies from 1 to 12. In order to prevent undue representation of the more fertile mothers, the mean fallow period preceding sibs born before propositi was calculated separately for each fraternity. The means of the mean fallow periods were then determined (Table V).

TABLE V

MEAN PREGNANCY-FREE INTERVALS (MONTHS) PRECEDING SIBS BORN BEFORE PROPOSITUS

Maternal Age (yrs) at Birth of Propositus	Under 25	25–	30–	35–	40 and over	All Ages
Mothers of Mongols	7·3 (3)	19·6 (17)	29·6 (22)	29·3 (41)	32·8 (61)	29·3* (144)
Mothers of Controls	4·5 (2)	17·3 (7)	31·8 (22)	32·6 (27)	38·5 (34)	32·7* (92)

Numbers of mothers are given in brackets.
Twelve mothers of mongols and eleven controls were unmarried at the commencement of first pregnancy and have been excluded.
* Standardized to the maternal age distribution of the combined series.

Standardization of the two series to the same distribution by maternal age at birth of propositi gives means of 29·3 and 32·7 months (difference 3·4 ± 2·8) for mothers of mongols and controls respectively. If all pregnancies, including those terminating in abortion, are taken into account, the means are reduced to 27·1 and 32·0 months. The difference (4·9 months) is increased, but is not large enough to provide firm evidence of a difference in fertility.

FERTILITY AFTER BIRTH OF A MONGOL.—The interval between the birth of a propositus and the date of the field inquiry ranged from less than one year to nearly 12 years. The length of this period obviously affects the number of subsequent sibs. Its effect on their preceding fallow periods is also important; its restriction would result in inadequate representation of the longer fallow periods. It is shown (Table VI) that the mongol and control series are not comparable in respect of year of birth of propositi, probably because of incomplete ascertainment of mongols in the earlier years. It is necessary, therefore, to standardize for this variable, as well as for the age of the mother at the birth of the propositus.

TABLE VI

YEAR OF BIRTH OF PROPOSITUS

Years	Mongols		Controls	
	No.	Per cent.	No.	Per cent.
1942–44	62	28·6	48	34·5
1945–48	78	35·9	49	35·3
1949–52	77	35·5	42	30·2
Total	217	100	139	100

The number of subsequent pregnancies is examined in Table VII. When the two series are made exactly comparable in respect of year of birth of propositi and maternal age, mean values of 0·36 and 0·34 viable pregnancies per mother are obtained for mothers of mongols and of controls respectively. The abortion rate is considerably higher after mongol than after control births (14·0 and 3·8 per 100 conceptions respectively). When abortions are included, the mean numbers of pregnancies for mothers of mongols and controls are 0·43 and 0·35 (difference 0·08 ± 0·08).

TABLE VII

PREGNANCIES FOLLOWING BIRTHS OF PROPOSITI

Maternal Age (yrs) at Birth of Propositus	Under 25		25–		30–		35–		40 and over		All Ages	
	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls	Mongols	Controls
No. of Mothers	14	14	36	21	40	29	59	39	68	36	217	139
No. of Subsequent Viable Pregnancies	12	10	20	9	20	16	18	14	4	2	74	51
Mean No. of Subsequent Viable Pregnancies*	0·79	0·71	0·62	0·33	0·50	0·55	0·33	0·39	0·06	0·06	0·36†	0·34†
No. of Subsequent Abortions ..	1	1	4	0	3	0	2	1	2	0	12	2
Mean No. of All Subsequent Pregnancies*	0·89	0·78	0·76	0·33	0·57	0·55	0·37	0·41	0·09	0·06	0·43†	0·35†

* Standardized to the distribution by year of birth of the combined series.
† Standardized to the distribution by year of birth and by maternal age of the combined series.

Of more interest, perhaps, is the duration of the pregnancy-free interval immediately following the mongol birth. In the mongol series, 62 propositi were followed by at least one conception within the period; in three cases precise dates were unknown. Corresponding figures for controls were 36 and two. After standardization for year of birth of propositus and for maternal age (Table VIII), the mean intervals between the birth of the propositi and the next conception were 21·6 months for the mongol fraternities and 21·4 months for the controls.

It is concluded that women who have given birth to mongols show no evidence of subsequent impairment of fertility.

TABLE VIII

MEAN PREGNANCY-FREE INTERVALS* BETWEEN BIRTHS OF PROPOSITI AND IMMEDIATELY SUCCEEDING CONCEPTIONS

Maternal Age (yrs) at Birth of Propositus	Under 25	25–	30–	35 and over	All Ages
Mothers of Mongols	20·0 (8)	24·5 (13)	25·0 (17)	17·3 (21)	21·6† (59)
Mothers of Controls	25·0 (6)	21·6 (6)	21·9 (12)	19·1 (10)	21·4† (34)

Numbers of mothers are given in brackets.

* Standardized to the distribution by year of birth of the combined series.

† Standardized to the distribution by year of birth and by maternal age of the combined series.

OTHER ASPECTS OF REPRODUCTIVE FUNCTION

Having considered reproductive performance as measured by the frequency with which conceptions occur, we turn now to the examination of other aspects of reproductive function. The relevant literature is most conveniently discussed in relation to the results of the present investigation.

AGE AT MENARCHE.—Age at onset of menstruation in mothers of mongols can be determined only by retrospective inquiry. The objections to this method are illustrated by an apparent correlation between age at menarche and age at birth of propositi (Table IX). It is probable that women tend to advance the date of menarche as they get older, and the impression that the menarche is delayed in women who later have mongols (Geyer, 1937; Doxiades and Portius, 1938) may have arisen in this way. The data support the view of Schröder (1938) that these women do not differ from other women in age at menarche.

TABLE IX

MEAN AGE AT MENARCHE

Maternal Age (yrs) at Birth of Propositi	Mothers of Mongols	Mothers of Controls
Under 25	13·15 (14)	13·37 (13)
25–..	13·92 (36)	13·25 (21)
30–..	13·72 (39)	13·33 (27)
35–..	14·02 (57)	14·22 (28)
40 and over ..	14·80 (66)	14·28 (36)
Mean Age* ..	14·11 (212)	13·84 (135)
Difference ..	0·27 ± 0·20	

Numbers of mothers are shown in brackets. Five mothers of mongols and four mothers of controls did not remember age at menarche.

* Standardized to the distribution by age at birth of propositi of the combined series.

MENSTRUAL HISTORY.—Although strictly reliable data can be obtained only from records kept for the purpose of inquiry, it was felt that interrogation of the mother as to her usual cycle length and duration of flow might give results which could be used for the present purpose. For mothers of mongols and controls respectively, mean cycle lengths were 28·86 and 29·50 days (difference: 0·64 ± 0·79), and mean duration of flow 5·16 and 5·01 days (difference: 0·15 ± 0·18). These results do not support the view that menstrual irregularities are of aetiological importance (Geyer, 1937; Doxiades and Portius, 1938).

Duration of post-partum amenorrhoea following birth of mongols was slightly shorter than that following the birth of control propositi (means 3·07 and 3·12 months respectively). The difference can be accounted for by the shorter duration of lactation after mongol births, due either to their early death or to difficulty in feeding; standardization of the two groups for this variable reverses the difference, which is not, however, sufficiently marked to invite comment (means: 3·10 and 2·71 months).

ONSET OF MENOPAUSE.—Periods of amenorrhoea and flushings were accepted as evidence of the menopause. One or both symptoms were experienced either before or within a year after the birth of the propositus by nineteen mothers of mongols and eight mothers of controls, all of whom were over 35 years old. Table X (overleaf) shows that mothers of mongols and mothers of controls who were in this age group at the birth of a propositus were well matched. This variable can therefore be ignored in examination of onset of the menopause. The incidence of menopausal symptoms was 15·6 per cent. (nineteen in 122 women) for mothers

of mongols and 11·3 per cent. (eight in 71) for mothers of controls (difference: 4·3 ± 5·2 per cent.) There is little difference between the two groups in respect of the mean ages of women who experienced menopausal symptoms (0·7 ± 1·2 years). The numbers are admittedly small, but a delayed menopause does not appear to be characteristic of women who have given birth to mongols. The view of Øster (1953) that the menopause occurs later in them than in the general population of women is not, of course, inconsistent with this conclusion. Any group of women identified by birth of a child in the later years of the reproductive period would probably show late onset of the menopause.

TABLE X

INCIDENCE OF MENOPAUSAL SYMPTOMS BEFORE OR LESS THAN A YEAR AFTER BIRTH OF PROPOSITI

Age (yrs) at Birth of Propositi	Mothers of Mongols		Mothers of Controls	
	No.	No. who had Menopausal Symptoms	No.	No. who had Menopausal Symptoms
36	13	1	8	0
37	14	1	8	0
38	17	3	8	1
39	10	2	11	1
40	18	2	6	0
41	18	2	14	3
42	11	3	7	2
43	10	1	4	0
44	4	2	2	0
45	4	0	0	0
46	2	2	1	0
47	1	0	1	0
48	0	0	1	1
Total	122	19	71	8
Mean age ..	39·9	40·8 (*a*)	39·8	41·5 (*b*)
Difference (*b*)–(*a*)	0·7 ± 1·2			

ABORTION RATES.—It has frequently been stated that mothers of mongols experience an abnormally high abortion rate with their other pregnancies (Murphy, 1936; Benda, Dayton, and Prouty, 1943; Beidleman, 1945; Engler, 1949; Benda, 1949). This view was not supported by Schröder (1938) or Penrose (1949). Two workers (Murphy, 1936; Penrose, 1949) who attempted comparison with a control group (consisting in each case of mothers of non-mongoloid defectives) obtained conflicting results, and the matter cannot be regarded as settled.

The subject has already received brief consideration in the discussion of fertility, where it was noted that mothers of mongols had a higher abortion rate than mothers of the control group. Before the data are examined in more detail it is desirable to ascertain whether the two groups are comparable in respect of number of conceptions.

It is shown (Table XI) that they are well matched, both in distribution according to number of conceptions and in the mean number of conceptions per woman.

TABLE XI

NUMBER OF CONCEPTIONS OF MOTHERS OF MONGOLS AND OF CONTROLS

No. of Conceptions* per Mother	Mothers of Mongols		Mothers of Controls	
	No.	Per cent.	No.	Per cent.
0	30	13·8	18	12·9
1	53	24·4	39	28·1
2	40	18·4	25	18·0
3 or 4	51	23·5	32	23·0
5 or 6	22	10·1	11	7·9
7 or more	21	9·7	14	10·1
Total	217	100	139	100
Mean No. of Conceptions	2·76		2·78	
Difference ..	0·02 ± 0·27			

* The conception which resulted in birth of a propositus is excluded.

Mothers of mongols had 600 conceptions, of which 64 (10·7 per cent.) were followed by abortion; control mothers had 386 conceptions with 26 (6·7 per cent.) abortions. (Pregnancies resulting in propositi are excluded.) The figures are not materially altered by standardization for maternal age. Some of the difference (4·0 ± 1·9) was due to a few women having had repeated abortions (Table XII). Nearly half the abortions experienced by mothers of mongols occurred in women who had more than one abortion; the corresponding proportion for control mothers was less than one-quarter.

TABLE XII

INCIDENCE OF ABORTIONS

No. of Abortions per Mother	Mothers of Mongols*			Mothers of Controls*		
	No. of Mothers	Per cent.	Total No. of Abortions	No. of Mothers	Per cent.	Total No. of Abortions
0	142	75·9	0	98	81·0	0
1	34	18·2	34	20	16·5	20
2	6			3		
3	3	5·9	30	0	2·5	6
4	1			0		
5	1			0		
Total ..	187	100	64	121	100	26

* Thirty mothers of mongols and eighteen control mothers who had had no conception except that resulting in the propositus have been excluded.

We have also inquired whether abortions are more frequent in the period preceding and following the birth of propositi. The numbers are insufficient to give an unequivocal answer; but the evidence gives little support for the view that abortion is particularly likely in the pregnancy immediately before or after the propositus (Table XIII, opposite).

TABLE XIII

INCIDENCE OF ABORTIONS ACCORDING TO PROXIMITY OF PROPOSITUS

Conceptions	Mothers of Mongols			Mothers of Controls			Difference
	No. of Conceptions	No. of Abortions	Abortion Rate (per cent.) (*a*)	No. of Conceptions	No. of Abortions	Abortion Rate (per cent.) (*b*)	(*a*)–(*b*)
Immediately Preceding or Succeeding Propositus	227	31	13·7	146	13	8·9	4·8 ± 3·4
Others	373	33	8·8	240	13	5·4	3·4 ± 2·2
Total	600	64	10·7	386	26	6·7	4·0 ± 1·9

UTERINE BLEEDING DURING PREGNANCY.—A high incidence of bleeding during the pregnancy resulting in the mongol has been reported (Geyer, 1937; Schröder, 1938; Beidleman, 1945; Ingalls, 1947; Benda, 1949), but comparison with a control group has not been attempted. In a retrospective inquiry, accurate reporting is impossible, and in examining the data we place more reliance on a comparison between the affected and control groups than on the actual incidence. Bleeding during the first 3 months of pregnancy was reported 23 times (10·6 per cent.) in respect of mongols and twelve times (8·6 per cent.) in respect of controls (difference 2·0 ± 3·2 per cent.). The difference is even smaller after standardization for maternal age and birth rank (1·7 per cent.).

GYNAECOLOGICAL DISORDERS.—Pelvic disorders for which specialist advice was obtained were reported by 48 of the 217 mothers of mongols (22·1 per cent.) and by thirty of the 139 control mothers (21·6 per cent.). The difference is quite insignificant and is scarcely altered by standardization for age or year of birth of propositi. Reasons for seeking advice (Table XIV) should be accepted with reserve, since the information is based on pátients' statements and was not confirmed from hospital records. No support is provided for the view of Ingalls (1947) that uterine retroflexion is of aetiological importance. The most notable feature of the Table is the difference in incidence of uterine fibroids, but in view of the small numbers and the possibility of under-reporting of the condition by the control mothers little importance can be attached to it.

TABLE XIV

REASONS FOR GYNAECOLOGICAL CONSULTATIONS

Condition	Mothers of Mongols		Mothers of Controls	
	No.	Per cent.	No.	Per cent.
Uterine Displacement ..	14	6·4	13	9·4
Uterine Fibroid	6	2·8	0	0·0
Conditions treated by Dilatation and Curettage	13	6·0	6	4·3
Other Specified Conditions	13	6·0	7	5·0
Unknown	2	0·9	4	2·9
Total	48	22·1	30	21·6

DISCUSSION

An increase in incidence with advancing maternal age is perhaps more firmly established and more striking in mongolism than in any other condition. It has been noted consistently in reported series, and shown to be largely, though not entirely, independent of the influence of birth order. There is thus good reason to believe that the maternal environment is important in the aetiology of mongolism, and attention has not unnaturally been directed to the changes which occur in the reproductive system as age increases (decline of fertility, increased incidence of abortions, the menopause, development of fibroids and other pathological conditions). The present inquiry provides little evidence of abnormalities in the reproductive system of mothers of mongols. Since this conclusion conflicts with some previous reports, we may briefly consider possible reasons for this variation.

Some investigators have attempted to explore the reproductive history without use of a control group; this procedure is evidently unreliable unless the incidence of abnormality is very high indeed. In two reports controls were used, but they consisted of mothers of non-mongoloid mental defectives who could not unreservedly be regarded as normal in respect of reproduction. But perhaps the most serious objection to most previous investigations has been failure to take full account of the influence of maternal age: most mothers of mongols are in the older age groups where the expected incidence of reproductive abnormalities is obviously raised. Unless a correction is introduced by standardization, or by the use of an age-matched control group, the frequency of abnormalities which become more common at late ages will inevitably appear to be raised. Jenkins (1933) is one of the few investigators who appear to have recognized this difficulty.

The present series is perhaps not large enough to permit firm conclusions concerning the aetiological significance of the variables examined (fertility, menstrual history, abortion rates, bleeding during pregnancy, and gynaecological disorders). The results suggest that some differences between mothers of affected and controls might emerge from a larger series: the fallow period preceding the birth of a mongol may be prolonged; habitual abortion may be more common; bleeding during pregnancy may occur more frequently. But if such differences exist, it seems unlikely that they will be large. The present investigation provides no evidence of any other abnormality in the reproductive history of mothers of mongols.

SUMMARY

(1) The reproductive histories of 217 Birmingham women who gave birth to a mongol in the period 1942–52 were compared with those of a control group of 139 women who produced unaffected infants during the same period. The two groups differed slightly with respect to age at birth of propositus; variation from this source was removed by standardization.

(2) The two groups showed little difference in fertility as measured by the number of conceptions preceding propositi, pregnancy-free intervals immediately before propositi and before prior sibs, number of conceptions following propositi, and pregnancy-free intervals between the birth of the propositus and the next conception.

(3) Mothers of mongols did not differ significantly from controls in respect of age at menarche, length of menstrual cycle, age at onset of the menopause, and uterine bleeding during the related pregnancy.

(4) Abortion rates were higher for mothers of mongols than for controls. This was due largely to the presence of a few women in the mongol group who experienced repeated abortions. Abortions were not unduly common in pregnancies immediately before or after that of the propositus.

(5) Gynaecological disorders were reported with equal frequency in the two groups.

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SOCIAL MEDICINE STUDIES BASED ON CIVILIAN MEDICAL BOARD RECORDS

III. PHYSICAL AND OCCUPATIONAL CHARACTERISTICS OF MEN WITH CERTAIN SKIN DISEASES

BY

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In a recent symposium on "Modern Trends in Dermatology", first place was given to a paper stressing the relevance of ecological factors to diseases of the skin (Banks, 1954). The conviction that such factors are important may nowadays be widespread, but there is still no statistical foundation for the belief. Mortality from cancer of the skin has been widely studied, but very little information is available concerning the prevalence of the less serious diseases which make up the bulk of dermatological practice. In the absence of any serious mortality from these diseases, death registration, the basis of the "social *post mortem*", has little of interest to contribute. Nor is the official collection of hospital statistics much help, for it refers only to in-patients (Registrar-General, 1954). It is reasonable, therefore, to turn to the ledgers kept by the Civilian Medical Boards, since these not only provide large numbers of case records but also enable them to be related to the population at risk. This is the course followed in the present study, which describes the distribution among men of military age (17–44 years) of four common types of skin disease (acne, eczema, dermatitis, and psoriasis). The sources of material and methods of analysis have been described in the first paper of this series (Stewart, Webb, and Hewitt, 1955a). The methods of calculation and the definition of Standardized Prevalence Ratios (S.P.Rs *passim*) are identical with those used in the study of varicose conditions (Stewart and others, 1955b).

MATERIAL

Table I shows the total number of cases recorded in three regions (Essex, Leicester, and Northampton). Previous work has shown that:

(1) it is unwise to put much weight on regional differences in the recorded prevalence of any disease which is compatible with reasonably good health,

(2) the relatively low prevalence rates in Northampton are probably due to under-recording of mild cases.

TABLE I

RECORDED PREVALENCE OF FOUR SKIN DISEASES AMONG MEN EXAMINED AT THREE CIVILIAN MEDICAL BOARD CENTRES (1941–44)

Area	Acne		Dermatitis		Eczema		Psoriasis	
	No.	Per 1,000	No.	Per 1,000	No.	Per 1,000	No.	Per 1,000
Essex	330	27·6	97	8·1	85	7·1	74	6·2
Leicester ..	975	42·0	140	6·0	209	9·0	92	4·0
Northampton..	413	26·2	71	4·5	69	4·4	39	2·5
All Areas ..	1,718	33·7	308	6·0	363	7·1	205	4·0

For the present purpose such differences are not important, since the method of calculating S.P.Rs allows for regional variation in standards of recording. *Within* each region, however, observed variations between age groups are of interest, for in this case independent results serve to corroborate *relative* prevalence rates even when the *absolute* rates are not strictly comparable.

FINDINGS

In each region the prevalence of *acne* was high in the youngest age group (17–19), and still higher in the second group (20–24), and thereafter declined rapidly. In each set of records the prevalence of *eczema* increased with age up to 40 yrs (by which time it was at least four times as common as in the late teens). *Dermatitis* maintained a comparatively even level from age to age. In all three regions, *psoriasis* showed a steep age gradient; the combined figures suggesting that this disease is some seven times as common among men in their early forties as

* In receipt of grant from the Medical Research Council.

among youths of 17–19. Unlike acne, psoriasis tends to persist or recur throughout life. Since it is rarely fatal (in the whole of England and Wales only forty deaths in the four years 1949–52 were ascribed to psoriasis and pityriasis rosea) and may manifest itself at any age, it follows that prevalence (as opposed to incidence) rates must increase with age. The unexpected steepness of the observed age gradient suggests one of two things. Either the disease had appeared for the first time in the twenties and thirties more often than would be expected from a perusal of standard text books, or the number of days per year on which affected persons showed signs which were worth recording had increased steadily with age.

BODY MEASUREMENTS.—Table II shows S.P.Rs for various divisions of the height, weight, and body-build scales on the original code.

TABLE II

STANDARDIZED PREVALENCE OF FOUR SKIN DISEASES IN RELATION TO HEIGHT, WEIGHT, AND BODY-BUILD

Group		Standardized Prevalence Ratios			
		Acne	Dermatitis	Eczema	Psoriasis
Height (in.)	Under 64	76	124	85	91
	64–	86	93	105	
	66–	101	108	95	95
	68–	106	90	95	100
	70–	114	95	121	127
	72–	119			
	P (χ^2)	<0·001	>0·30	>0·30	>0·20
Weight (lb.)	Under 120	76	100	83	80
	120–	93	91	88	104
	130–	98	121	97	118
	140–	110	90	117	105
	150–	128	103	97	89
	160–	141	83	138	
	P (χ^2)	<0·001	>0·30	<0·10	>0·30
Body-Build Ht/$\sqrt[3]{}$Wt (approx.)*	12·2	129	86	116	93
	12·6	101	100	96	89
	12·9	106	116	92	
	13·2	96	110	107	86
	13·5	101	91	103	118
	13·9	86	80	76	151
	P (χ^2)	<0·01	>0·50	>0·30	<0·10

* The scale 12·2–13·9 represents gradation from stocky to slender build.

It will be seen that risk of *acne* increased significantly with height and also with weight. On balance, the association with weight was the stronger, as is shown by the high S.P.R. (129) for men with the most rotund body-build (*i.e.* those with a Ht/$\sqrt[3]{}$Wt index of approximately 12·2). The highest risk was, however, found among the heaviest men, *whether or not* they were overweight for their height. The full range of variation was even greater than that shown in Table II, the S.P.Rs rising from 64 for men of less than 110 lb. to 165 for men of 170 lb. or over. The six ratios shown in Table II are so nearly co-linear (linear correlation coefficient between S.P.R. and weight = + ·99) that it seems appropriate to describe the dependence of risk on weight by the linear equation of best fit. This was found to be:

$$R_{(A)} = 1{\cdot}08\,W - 45{\cdot}2$$

where W refers to weight in pounds and $R_{(A)}$ to the risk of acne, expressed as a percentage of the risk for all men of a given age. A similar relationship was found when S.P.Rs were calculated separately for each area. It was also found to hold good for men in their late twenties and thirties as well as for the younger, more susceptible age groups.

Neither *dermatitis* nor *eczema* yielded any significant correlation with body measurements, though the latter condition showed a suggestively low prevalence among light men.

The only other definite finding in relation to body measurements was an association between *psoriasis* and slender build, as indicated by the S.P.R. of 151 for men with a Ht/$\sqrt[3]{}$Wt ratio of approximately 13·9. The number of cases of psoriasis was much smaller than those of the other diseases, and the result, as shown in Table II, is not statistically significant, but a conventional level of significance can be achieved by reducing the number of degrees of freedom in the χ^2 test.

SOCIAL CLASS.—Table III compares the prevalence of the four skin diseases among men of different social class.

TABLE III

COMPARATIVE PREVALENCE OF FOUR SKIN DISEASES IN THE REGISTRAR GENERAL'S SOCIAL CLASSES

Social Class	Standardized Prevalence Ratios					
	Acne			Dermatitis	Eczema	Psoriasis
	All Ages	17–24	25–44			
I and II ..	105	114	95	61*	105	89
III ..	100	103	94	99	99	102
IV ..	108	102	119	89	92	95
V	89	73**	125	148***	110	103
Value of χ^2 for 3 d.f.	4·011	12·032	7·663	14·306	0·822	0·431
P (χ^2) ..	0·30–0·20	0·01–0·001	0·10–0·05	0·01–0·001	0·90–0·80	0·95–0·90

* Significant at the 0·05 per cent. level.
** Significant at the 0·02 per cent. level.
*** Significant at the 0·05 per cent. level.

Three sets of S.P.Rs for *acne* are given because of contrary findings for younger and older age groups. Thus young men from the labouring classes were

only half as likely to suffer from acne as young men from the professional classes. After the age of 25, however, the highest prevalence was at the lowest end of the social scale. S.P.Rs for Social Classes IV and V show that this reversal of the social gradient occurred independently in all three regions:

Social Class	Region	Age Group	
		17–24	25–44
IV and V..	Leicester	90	122
	Northampton ..	85	111
	Essex	84	125
All ..	All	100	100

The dual relationship between acne and social class probably has a simple dietary-cum-occupational explanation. Stein (1947) reported the complete disappearance of acne in a concentration camp and its reappearance on liberation. In normal life it is likely that a plain diet keeps down the prevalence of non-occupational cases (*i.e.* acne vulgaris), but with advancing age acneiform eruptions which result from exposure to external irritants (*e.g.* chloracne) must form a higher proportion of the total. This may be the reason why acne appears to be, at one and the same time, a disease of affluence and of poverty.

Among the older men examined by Civilian Medical Boards the prevalence rates for *acne* and *dermatitis* tended towards a similar social class distribution, but the contrast between unskilled and professional classes (which was of similar magnitude in the three sets of records) was consistently greater for dermatitis than for acne.

Neither *eczema* nor *psoriasis* showed the least sign of deviating from an even prevalence in all levels of society.

OCCUPATION.—Table IV summarizes the findings relating to occupation. The twelve groups shown in this Table are clearly too heterogeneous for a precise study of occupational dermatoses. But although lack of numbers precluded the calculation of separate S.P.Rs for many occupations distinguished in the original code, several quite small groups were identified with high risks. Thus the excess of *acne* in textile workers was eventually traced to the men engaged on bleaching and dyeing (S.P.R. 142), and that in the mixed building and farming group to farm workers (S.P.R. 73 at ages 17–24 and 173 at ages over 25). Exceptionally high rates for acne were also observed among the central lathe turners who are exposed to mineral oils (seventeen cases in Leicester compared with seven "standard" cases), and for a sub-group of the Registrar-General's Order XIII (*i.e.* Makers of products not specified elsewhere but excluding workers in rubber) the S.P.R. for acne was 219. This group includes workers in plastics, among whom occupational skin disease has previously been reported (Schwartz, Tulipan, and Peck, 1947).

TABLE IV

COMPARATIVE PREVALENCE OF FOUR SKIN DISEASES IN TWELVE OCCUPATIONAL GROUPS†

Occupational Group	Acne			Dermatitis	Eczema	Psoriasis
	All Ages	17–24	25–44			
Professional, Administrative	112	153***	85	D	E	D
Commercial ..	93	91	98	78	111	D
Clerical ..	101	112	D*	D*	113	D
Boot and Shoe	93	93	93	79	108	112
Textile ..	122*	129	117	D	115	118
Metal manufacture	105	113	79	121	80	132
Trade not defined‡	98	87	132	101	98	D
Warehouse ..	97	109	81	E	D	D
Transport ..	94	96	89	115	86	E
Building and Agriculture	94	85	109	130	87	D
Unskilled ..	91	72***	138*	156***	102	D
Other.. ..	109	109	108	97	94	91
Value of χ^2 for 11 d.f. ..	12·727	29·123	20·807	27·815	4·357	6·032
$P(\chi^2)$.. ..	0·50–0·30	<0·01	0·05–0·01	<0·01	0·98–0·95	0·90–0·80

† Individual occupations were considered to be significantly different from standard if their contribution to the sum of χ^2 for all occupations would have been significantly large in a test based on 1 d.f.; these are marked by asterisks (see Table III).

‡ Occupations common to several trades (e.g. fitters, cutters, inspectors, etc.).

By and large, unskilled labourers had a higher prevalence of *dermatitis* than men who had learnt a particular trade, but the ratio for builders (S.P.R. 177), who are known to suffer from cement dermatitis, was even higher than for unskilled workers. No evidence was found of any occupational factor affecting the prevalence of *eczema* or *psoriasis*.

At the outset of the investigation some doubt had been felt about the propriety of attempting a separate analysis of the records of eczema and dermatitis since it was thought that the examining doctors might have used these terms indiscriminately or have had difficulty in distinguishing industrial dermatitis from idiopathic eczema. It is therefore interesting to observe that the conditions labelled dermatitis and eczema were in fact quite sharply differentiated from one another by social and occupational features as well as by age distribution.

DISCUSSION

The principal finding of the section on physical measurements is the relationship between weight

and risk of acne. It must at first seem surprising that a disease which is influenced by endocrine factors did not reveal a stronger correlation with body-build than with absolute size, but it may be that (of the three variables used in this section) weight most adequately represents the measure which has the greatest relevance to skin function, namely, the ratio of weight to surface area. Discussing the best method for determining the surface area of subjects of metabolism experiments, Du Bois (1936) says:

> In dealing with people of normal build and particularly in dealing with the averages of large numbers of persons of normal build, it makes no difference whether one uses $11 \cdot 0\ W^{2/3}$ . . . or employs a method involving both height and weight.

It follows that the ratio of weight to surface area would, on average, be proportional to the cube root of weight. Over the range 100 to 200 lb. any linear dependence of risk upon this ratio would be indistinguishable from linear dependence on weight *per se*. Thus body-weight, by measuring (however indirectly) the "load" on the sebaceous glands, could be a measure of acne risk, just as height (by indicating the "load" on the inferior vena cava and its branches) has proved to be a measure of varicosity risk (Stewart and others, 1955b).

Though the smaller numbers did not support any firm conclusion with regard to eczema, there was some resemblance between the physique distribution of this disease and that of acne. For the result which most nearly approached statistical significance was that relating to weight, with a general tendency for prevalence to increase with increasing weight.

It is not so easy to offer a physiological explanation for slender individuals being excessively prone to psoriasis. This, however, is a disease in which hereditary influences are thought to play an important role, and it may be that an inherited tendency to slender build is linked with the psoriatic diathesis. This hypothesis could be tested by comparing the body measurements of patients with and without a family history of the disease.

Sheldon and his associates believe that skin diseases tend to be associated with "cerebrotonia" and thus, by implication, with ectomorphic build (Sheldon, Stevens, and Tucker, 1940). Since a high value of the index $Ht \div \sqrt[3]{Wt}$ is a definite indication of ectomorphy, the present findings for psoriasis accord with this view. On the other hand, the findings for acne, dermatitis, and eczema are incompatible with such expectations.

In view of the known association between asthma and eczema, it is perhaps worth mentioning that in unpublished analyses of the present set of Civilian Medical Board records a very strong association was found between prevalence of asthma and light weight. Eczema, on the other hand, was less common among the light men. Asthma also appeared to be a disease of affluence (the S.P.Rs being 172 for Social Class I and II, 98 for Social Class III, 84 for Social Class IV, and 66 for Social Class V), although the cases of eczema were distributed regardless of social class. It is arguable that the body-build contrasts are misleading, and that they are really due to the fact that asthma *causes* loss of weight. It is, however, certain that, whatever the common factor in asthma and eczema may be, it is not closely linked with social status.

Summary

A study has been made of the physical and occupational characteristics of several hundred men who, at the time of their pre-service medical examinations, were suffering from acne, dermatitis, eczema, or psoriasis.

Acne was found to be especially prevalent in men of Social Class I and II in the age group 17–24, but at ages over 25 it was more common among the unskilled classes. At all ages there was a positive correlation between prevalence of acne and body-weight.

Psoriasis was found to be associated with slender build, but not with occupation or social status.

No significant variations were found in the prevalence of eczema, except with respect to age.

Dermatitis was particularly common among builders and unskilled workers but was not related to height and weight or body-build.

The significance of these findings is discussed with reference to somatotyping and to the eczema-asthma syndrome.

We should like to record our thanks to the Nuffield Provincial Hospitals Trust and the Medical Research Council, who contributed generously towards the expenses of the investigation. We are also indebted to Dr. F. Acheson, Dr. W. Boake, Dr. A. E. Naish, Dr. J. Parfit, and Dr. M. Russell, who gave valuable assistance in the coding of the medical data.

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EMPLOYMENT OF RECOVERED TUBERCULOUS PATIENTS

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Under ideal conditions, successful treatment for tuberculosis should be followed by a period of rehabilitation during which the patient gradually returns to full-time suitable employment. Often, however, for economic and other reasons, the provision of adequate facilities for rehabilitation is not easily realized and consequently many patients are left more or less to their own initiative in finding subsequent remunerative work. With a view to discovering what happens in such circumstances, a postal survey of recovered tuberculous patients was carried out recently in Northern Ireland.

In Northern Ireland there are at present no Remploy factories or village settlement for tuberculous patients. A small rehabilitation department has been established by the Northern Ireland Tuberculosis Authority, but apart from this, little exists to meet this particular need. The group surveyed, therefore, represents patients who have been left to their own devices in the post-recovery period.

Material

From the beginning of 1948 (the first complete calendar year of operation of the Northern Ireland Tuberculosis Authority) until the end of 1952, there were 953 known recovered cases of tuberculosis. It was not possible to include all the recovered cases in the survey because of the time and cost involved, and instead a sample of 200 (91 males, 109 females) was selected by means of random numbers. To each of these individuals a letter, questionnaire, and business reply envelope were sent, followed—if necessary—by two reminder letters at fortnightly intervals. For various reasons 35 forms were not completed.*

Using the χ^2 test for significance and adopting the conventional level of probability of $P < 0{\cdot}05$ (the criterion used throughout the report), no significant differences were found in respect of age, sex, tuberculosis classification, and locality between the population of 953 persons from which the sample was drawn and:

(*i*) the 165 persons who replied, including nine children;

(*ii*) the 35 persons who failed to reply.

Persons who failed to reply differed, however, from those who did reply in respect of duration of illness, and this topic has not been studied.

In the following Tables the nine children (all under 12 years of age) have been excluded, leaving a final sample of 156 (74 males and 82 females; 131 pulmonary and 25 non-pulmonary).

Results

A summary of the employment situation is given in Table I. Allowing that housework counts as an occupation, there was no significant difference between the two sexes in respect of numbers employed. Over 50 per cent. of the sample were gainfully employed (full or part-time), 28 per cent. were in unpaid work (housewives), and almost 20 per cent. were not working.

TABLE I

DISTRIBUTION OF SAMPLE MEMBERS BY SEX AND EMPLOYMENT

Group	Males		Females		Total	
	Number	Per cent.	Number	Per cent.	Number	Per cent.
Employed	51	68·9	23	28·0	74	47·4
Unemployed ..	23	31·1	8	9·8	31	19·9
Housewife-only ..	—	—	44	53·7	44	28·2
Housewife in paid employment ..	—	—	7	8·5	7	4·5
Total	74	100·0	82	100·0	156	100·0

From the Ministry of Labour estimates (*Ministry of Labour Gazette*, 1953) it was calculated that approximately 297,600 insured men and 169,000 insured women in Northern Ireland were employed at the time of the survey and 33,500 insured men

* Eleven persons failed to reply, six had emigrated, three had died, five stated that they had never had tuberculosis, four did not complete the form because of age or incapacity, and in six cases the correct address could not be traced.

and 14,700 insured women were unemployed. Excluding five men and three women in the sample who were likely to be outside the scope of the National Insurance Scheme, the percentage of unemployed in the sample was 33·3 males and 28·6 females. These figures may be contrasted with 10·1 per cent. for unemployed males and 8 per cent. for unemployed females in the general population. It would appear, therefore, that the level of employment among "cured" tuberculous patients is much lower than the general level of employment in Northern Ireland.

Following the Ministry of Health's Classification (Ministry of Health, 1947), a comparison was made between "early" (A1) and "more advanced" (A2, 3; B1, 2, 3) cases of pulmonary tuberculosis (Table II).

TABLE II

DISTRIBUTION OF EMPLOYED AND UNEMPLOYED SAMPLE MEMBERS BY CLASSIFICATION OF DISEASE

Classification	Employed	Unemployed	Total
Early (A1)	38	13	51
Remainder (A2, 3; B1, 2, 3)	22	14	36
Total	60	27	87*

$\chi^2 = 1{\cdot}22$, $N = 1$, $0{\cdot}30 > P > 0{\cdot}20$

* Excluding eighteen cases of non-pulmonary tuberculosis.

Contrary to what might have been expected, the chronicity of the disease did not appear to have influenced the employment situation. There was, however, a slightly higher level of employment among the "early" cases (74·5 per cent) than among the remainder (61·1 per cent.). The unemployed group comprised 48 per cent. A1 cases and 52 per cent. "more advanced" cases.

A comparison between the employed and unemployed persons in (*a*) urban and rural areas, and (*b*) Belfast and elsewhere, failed to reveal any significant difference. Though the findings are based on very small numbers, they suggest that place of domicile in Northern Ireland does not materially influence a tuberculous patient's opportunities for employment.

Information was obtained as to the general standard of education of the sample members (Table III). As might be expected there was a higher percentage of employment among persons who had obtained post-primary schooling, than among those who had only attended elementary schools, but the numbers are too small for the differences to be statistically significant.

TABLE III

DISTRIBUTION OF EMPLOYED AND UNEMPLOYED SAMPLE MEMBERS BY EDUCATION

Education	Employed	Unemployed	Total
Primary	48	25	73
Post-Primary	26	6	32
Total	74	31	105

$\chi^2 = 1{\cdot}88$, $N = 1$, $0{\cdot}20 > P > 0{\cdot}10$

In Table IV all occupations placed by the Registrar - General (Registrar - General, 1951) in Social Classes I, II, IIIc, IIId, and IIIe are grouped together as "light" work and the remaining occupations (*i.e.* Social Classes IIIa, IIIb, IV, and V) as "heavy" work. In 21 cases (ten males and eleven females) no information about previous work was obtained, but for the 53 cases with records of pre- and post-illness employment, there was very little evidence of movement between "light" and "heavy" work. On the whole, the tendency was for patients to return either to the same or to a similar type of employment. In fact, in 34 cases, the occupation resumed after cure was identical with the one held before the patient became ill. This feature of the employment situation applied to all types and grades of work (*e.g.* agricultural and other labourers, managers, cutters, roundsmen, clerks, etc.).

TABLE IV

DISTRIBUTION OF EMPLOYED SAMPLE MEMBERS BY TYPE OF WORK BEFORE AND AFTER ILLNESS

		Work before Illness		
		Heavy	Light	Total
Work after Illness ..	Heavy ..	15	4	19
	Light ..	2	32	34
	Total ..	17	36	53

Three persons failed to answer the question, "Do you find your work tiring?"; 25 answered in the affirmative and 46 gave negative replies. Of those who said they were tired, fifteen were in "light" and ten in "heavy" occupations. Of those who denied being tired by their work, 33 were in "light" and thirteen in "heavy" occupations. Because of the small numbers involved, it is impossible to draw any firm conclusions from these findings, but the fact that tiredness was slightly more common in the "heavy" occupations suggests that the two factors may be related.

The mean working week for men was 45·8 hours (*i.e.* just over 8 hours per day for 5½ days per week)

with a standard deviation of 6·80. For the women in gainful employment, the mean was 43·3 hours and the standard deviation 10·15. There is, therefore, no significant difference between the sexes in the hours worked per week.

Only one of the 31 unemployed persons had any immediate prospect of returning to work. Five were not fit for any kind of work, nine desired full-time work, eleven would have been content with full or part-time work, four wanted part-time work only, and two did not answer the question. Three persons gave as their first choice their previous occupation, but although the group as a whole favoured sedentary jobs no single occupation emerged as favourite.

Replies were received from 51 married women. Of these 44 were doing housework only and seven combined housework with a paid job. The average number of persons in each household was 4·4 for housewives only, and three for housewives in paid work.

The housewives only averaged just over eight hours per day and the housewives in paid work averaged (outside the home) a 44-hour week.

Eleven of the housewives only expressed a desire for other employment, usually of a domestic nature. Only two of the housewives in paid employment admitted to having assistance with the housework. Although the numbers are small, it seems likely that the size of the family and the ability to procure domestic help are both important facts, in determining whether or not married women seek outside employment.

Summary

(1) The results of a postal survey of recovered tuberculous patients living in Northern Ireland are given. The object of the survey was to discover what happens to tuberculous patients when left free to find their own employment.

(2) Originally, the sample consisted of two hundred persons (drawn from a population of 953 known recovered cases), but for a number of reasons 44 were rejected or did not respond, thus leaving 156 persons (78 per cent.) who completed questionnaires.

(3) Of the 156 persons, 74 (47·4 per cent.) were employed, 31 (19·9 per cent.) were unemployed, and 51 (32·7 per cent.) were housewives.

(4) A much higher level of unemployment existed amongst ex-patients than in the community at large.

(5) The chronicity of the disease of the recovered tuberculous person did not appear to have any significant influence upon the employment situation.

(6) The place of domicile in Northern Ireland did not confer any particular advantage.

(7) On the whole, the tendency was for patients to return either to the same or similar type of employment. This was the case in 64 per cent. of the employed persons.

(8) Of the unemployed persons, 80·7 per cent. had no prospects of securing any kind of work; the majority of this group expressed a desire for "light" work.

(9) Data were collected in respect of 51 housewives and of these 44 were occupied solely on housework, while seven had undertaken paid work in addition to their household duties.

(10) The survey suggests that almost one-quarter of all recovered cases require special assistance if they are to obtain suitable employment. Rehabilitation programmes for tuberculous patients should not overlook this.

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A FURTHER STUDY OF A–B–O BLOOD GROUPS AND DIFFERENTIAL FERTILITY AMONG WOMEN IN TWO AUSTRALIAN MATERNITY HOSPITALS

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Two previous reports have examined certain aspects of the problem of incompatibility between mother and child with respect to the A-B-O blood groups for samples drawn from Australian Maternity hospitals. In the first of these, Bryce and others (1950) examined the mother-child blood-group combinations for 7,909 women confined in the Queen Victoria Hospital, Melbourne, during the years 1944–48. In certain mother-child combinations they observed striking differences from expectation. These differences were significant for the excess over expectation of group A infants born to group B mothers, and for the deficiency of group AB infants born to group A mothers. There was also a marked, but not significant, deficiency of group A infants to group O mothers. The analysis suggested also the possibility that AB women are more fertile than women belonging to other blood groups.

The second study, by Kirk and others (1953), examined the pregnancy experience of women of different blood groups confined in the King Edward Memorial Hospital, Perth, during the years 1948–51. A polynomial function fitted to the difference in the average number of pregnancies between women of group O and group A for each year of age from 16–40 showed a significant excess of pregnancies in group A women between the ages of 25 and 35, with a tendency for group O women to equal or surpass group A women over the age of 35. These authors suggested that the excess of pregnancies in group A women in the decade centred in age 30 might be due to the selective loss of children to group O women in incompatible mating groups, and that group O women in compatible mating groups are more fertile, and their child-bearing activities more prolonged than those of group A women.

Since these reports were published, we have been able to add further material to both the Melbourne and Perth samples. These cities differ appreciably in size and social structure, and the reproductive patterns of the women in the two samples are significantly different. We thought it desirable therefore to analyse this extended material so that similarities and differences would be emphasized. Certain information was not always available for both samples for the whole of the period under study. In addition the heavy immigration of non-English people into Australia during the post-war years has introduced a heterogeneity into the samples for which due allowance must be made if errors in deduction are to be avoided. Despite these difficulties, however, the results recorded below indicate the value of this type of analysis in studying the effects of blood-group incompatibility on pregnancy experience.

METHODS

The source of the samples, and the techniques of collecting data and determining blood-groups have been given in detail by Bryce and others (1950) and Kirk and others (1953). In addition to the samples analysed in these two papers, 8,423 women were added to the Melbourne sample and 3,831 women added to the Perth sample during the years 1952 and 1953. The complete Melbourne sample therefore comprises 16,332 confinements for the years 1944–48 and 1952–53, the corresponding figure for the Perth sample being 9,952 confinements during the 6 years 1948–53.

Results

(1) *Differences in Composition of Samples.*—The Melbourne 1944–48 and the Perth 1948–51 samples have been analysed in detail previously (Bryce and others, 1950; Kirk and others, 1953). No information was available for the earlier Melbourne sample with respect to mother's age or parity, and whether she was of English or non-English name. Tables I–III give the basic data for the 1952 and 1953 sample for both Melbourne and Perth.

In both Melbourne and Perth samples there is a highly significant difference in the blood-group distributions for women of English and non-English name ($\chi^2 = 23{\cdot}857$ and $26{\cdot}081$ respectively for 3 *d.f.*). There is no dignificant difference for the English name samples between Melbourne and Perth ($\chi^2 = 7{\cdot}009$ 3 *d–f*), or for the non-English name samples ($\chi^2 = 3{\cdot}833$ 3 *d–f*).

Although the blood-group frequencies for women of English name are not significantly different in the two samples, there is a significant difference in the age distribution of women entering the two hospitals (Table III, $\chi^2 = 33{\cdot}878$ on 4 *d–f*). The same is true also for women of non-English name ($\chi^2 = 23{\cdot}316$ on 4 *d–f*). For the English name sample the difference is due largely to the increased number of young mothers in Perth. The women of non-English name are significantly older in the two samples than those of English name. This is readily understood, since many of them are recent immigrants to Australia and their reproductive experience has been more seriously interfered with by war and its aftermath than is the case for the women of English name. Most of the latter have been resident in Australia since birth. (The validity of this statement has been

Table I

COMPOSITION OF THE 1952–53 SAMPLES FOR MELBOURNE AND PERTH

Blood Group of Mother	Melbourne				Perth			
	Single Births	Twin Births	Rank and Age not Stated	Total	Single Births	Twin Births	Rank and Age not Stated	Total
O	3,741	54	118	3,913	1,780	20	—	1,800
A	3,202	31	102	3,335	1,505	18	—	1,523
B	801	11	38	850	396	6	—	402
AB	306	4	15	325	104	2	—	106
All Groups	8,050	100	273*	8,423	3,785	46	—	3,831

* Five of these cases had no age stated, but pregnancy rank was recorded. They have been included in the single birth analysis by rank.

Table II

DISTRIBUTION OF ABO BLOOD GROUPS AMONG MOTHERS OF ENGLISH AND NON-ENGLISH NAME IN TWO AUSTRALIAN MATERNITY HOSPITAL SAMPLES

Blood Group	Melbourne, 1952 and 1953						Perth, 1952 and 1953					
	English Name		Non-English Name		Total Sample		English Name		Non-English Name		Total Sample	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
O	3,196	47·22	599	43·37	3,795	46·56	1,384	48·17	416	43·42	1,800	46·99
A	2,697	39·84	536	38·81	3,233	39·67	1,153	40·13	370	38·62	1,523	39·75
B	632	9·34	180	13·04	812	9·96	262	9·12	140	14·61	402	10·49
AB	244	3·60	66	4·78	310	3·80	74	2·58	32	3·34	106	2·77
All Groups	6,769	100·00	1,381	100·00	8,150	99·99	2,873	100·00	958	99·99	3,831	100·00

Table III

AGE DISTRIBUTION OF MOTHERS OF ENGLISH AND NON-ENGLISH NAME IN TWO AUSTRALIAN MATERNITY HOSPITAL SAMPLES

Age Group (yrs)	Melbourne, 1952 and 1953						Perth, 1952 and 1953					
	English Name		Non-English Name		Total Sample		English Name		Non-English Name		Total Sample	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
20 and under	1,094	16·16	158	11·44	1,252	15·36	581	20·22	112	11·69	693	18·09
21–25 ..	2,492	36·81	488	35·34	2,980	36·56	1,043	36·30	279	29·12	1,322	34·51
26–30 ..	1,780	26·30	454	32·87	2,234	27·41	666	23·18	314	32·78	980	25·58
31–35 ..	919	13·58	200	14·48	1,119	13·73	346	12·04	152	15·87	498	13·00
36 and over	484	7·15	81	5·87	565	6·93	237	8·25	101	10·54	338	8·82
All Ages ..	6,769	100·00	1,381	100·00	8,150	99·99	2,873	99·99	958	100·00	3,831	100·00

checked for a single year in the Perth sample by examining the information recorded on the birth certificates of all babies born in the King Edward Memorial Hospital during 1952*).

Because of the difference in age structure between the two samples we have considered it important to analyse the data from Melbourne and Perth separately.

(2) *Mean Number of Pregnancies per Woman.*—It has been possible to calculate the mean number of pregnancies for women of English name in the Melbourne sample for 1952 and 1953 and in the Perth sample for the whole period 1948–53 (Table IV). In both places women of group A have experienced more pregnancies on the average than group O women. In the Melbourne sample the difference of 0·055 pregnancies per woman is not significant ($t = 1·271$) but the difference in Perth of 0·103 pregnancies per women is significant at the 5 per cent. level ($t = 2·296$).

TABLE IV

MEAN NUMBER OF PREGNANCIES PER WOMAN IN EACH BLOOD GROUP

(Women of English Name only)

Blood Group	Melbourne, 1952 and 1953			Perth, 1948 to 1953		
	No. of Women	Mean No. of Pregnancies	S.D. of Mean	No. of Women	Mean No. of Pregnancies	S.D. of Mean
O	3,196	2·503	0·029	3,711	2·702	0·030
A	2,697	2·558	0·033	3,281	2·805	0·033
B	632	2·429	0·062	755	2·767	0·069
AB	244	2·508	0·108	205	2·756	0·126
All Groups	6,769	2·518	0·020	7,952	2·752	0·021

It is of interest to note that the mean number of pregnancies for AB women in these two samples is lower than group A in one and than both group A and group B in the other. These figures do not lend support therefore to our earlier suggestion (Bryce and others, 1950) that AB women might be more fertile than women in other blood groups.

(3) *Mean Number of Pregnancies for Group O and A Women at Different Ages.*—In Table V (opposite) the mean number of pregnancies for group O and A women is given for age from 16–40 yrs. If the difference between the means for group O and group A women is plotted, it is possible to fit a curve to the values obtained. For the Perth sample the difference tends to increase linearly with age, and in the fitted curve the linear term accounts for the bulk of the variation. Unlike the earlier and smaller Perth sample, there is no longer any apparent tendency for group O women to compensate over the age of 35 for the clear-cut deficiency in pregnancy experience of group O women between the ages of 25–35. We can conclude, therefore, that in the Perth 1948–53 sample, women of group A have experienced relatively more pregnancies than group O women: not only is the difference in the means significant, but the difference increases linearly with age.

A similar analysis applied to the difference in mean number of pregnancies experienced by women of English name of groups A and O in the Melbourne 1942–53 sample shows no consistent trend, only the quintic term in the polynomial having any significance. At first this result seems surprising, since the Perth and Melbourne samples are approximately the same size. A more detailed examination of the data in Table V reveals that a trend similar to that present in the Perth sample is present in the earlier age groups, but the variation from year to year above age 35 becomes very great in the Melbourne sample. In fact the polynomial fitted to the differences between group A and group O women from age 16 to 33 reveals a significant trend, the linear and quadratic terms accounting for the bulk of the variation. It should be pointed out clearly, however, that even though the trend in pregnancy experience in the younger age groups is the same in both the Melbourne and Perth samples, the difference between group A and group O women in Melbourne is never as large as is the case in Perth.

It seems likely that the discrepancy between the analysis for the Perth and Melbourne samples is related to the difference in the overall pregnancy experience of women in the two samples. The Perth women of English name have had 0·23 more pregnancies per woman than the corresponding women in Melbourne, the difference being highly significant ($t = 7·97$, $P < 0·001$). The difference in pregnancy experience between group O and group A women will almost certainly be less marked in the sample with the smaller average number of pregnancies per woman. The importance of bearing in mind the difference in pregnancy experience when comparing the relationship of blood groups to fertility in samples from difference places will be discussed more fully in a later section.

(4) *Mother-Child Blood-Group Combinations.*—For the Melbourne sample the blood-group of the child has been determined in addition to that of the

* We are indebted to the Registrar-General for Western Australia for permission to search his records.

TABLE V

MEAN NUMBER OF PREGNANCIES TO GROUP O AND A WOMEN OF ENGLISH NAME ONLY AT DIFFERENT AGES

(Melbourne, 1952 and 1953; Perth 1948 to 1953)

Age of Mother (yrs)	Melbourne, 1952 and 1953						Perth, 1948 to 1953					
	Group O Rh + and −			Group A Rh + and −			Group O Rh + and −			Group A Rh + and −		
	No. of Women	No. of Pregnancies	Mean No. of Pregnancies	No. of Women	No. of Pregnancies	Mean No. of Pregnancies	No. of Women	No. of Pregnancies	Mean No. of Pregnancies	No. of Women	No. of Pregnancies	Mean No. of Pregnancies
16 or less ..	23	23	1·0000	25	26	1·0400	33	37	1·1212	18	18	1·0000
17	70	77	1·1000	33	37	1·1213	79	90	1·1392	73	77	1·0548
18	97	118	1·2165	78	94	1·2051	152	187	1·2303	137	164	1·1971
19	143	204	1·4266	138	195	1·4130	233	319	1·3691	202	281	1·3911
20	197	304	1·5431	151	235	1·5563	282	434	1·5390	255	409	1·6039
20 and under	530	726	1·3698	425	587	1·3812	779	1,067	1·3697	685	949	1·3854
21	232	396	1·7069	194	329	1·6959	289	512	1·7716	247	465	1·8826
22	232	439	1·8922	202	394	1·9505	288	551	1·9132	247	490	1·9838
23	236	454	1·9237	198	407	2·0556	260	576	2·2154	245	518	2·1143
24	247	516	2·0891	199	444	2·2312	269	629	2·3383	221	543	2·4570
25	213	486	2·2817	207	481	2·3237	232	588	2·5345	206	514	2·4951
21–25 ..	1,160	2,291	1·9750	1,000	2,055	2·0550	1,338	2,856	2·1345	1,166	2,530	2·1698
26	219	540	2·4658	199	519	2·6080	219	597	2·7260	169	475	2·8107
27	191	504	2·6387	151	388	2·5695	200	595	2·9750	172	518	3·0116
28	152	465	3·0592	127	386	3·0394	163	537	3·2945	148	498	3·3649
29	138	404	2·9275	112	344	3·0714	144	465	3·2292	137	518	3·7810
30	133	440	3·3083	117	366	3·1282	113	399	3·5310	126	511	4·0556
26–30 ..	833	2,353	2·8247	706	2,003	2·8371	839	2,593	3·0906	752	2,520	3·3511
31	110	383	3·4818	97	325	3·3505	106	422	3·9811	105	413	3·9333
32	114	415	3·6404	93	306	3·2903	104	381	3·6635	108	432	4·0000
33	76	279	3·6711	69	247	3·5797	79	328	4·1519	72	307	4·2639
34	72	266	3·6944	56	220	3·9286	64	260	4·0625	65	312	4·8000
35	66	242	3·6667	47	167	3·5532	63	292	4·6349	60	271	4·5167
31–35 ..	438	1,585	3·6187	362	1,265	3·4945	416	1,683	4·0457	410	1,735	4·2317
36	61	252	4·1311	43	169	3·9302	74	347	4·6892	53	269	5·0755
37	44	183	4·1591	42	198	4·7143	51	263	5·1569	59	305	5·1695
38	41	157	3·8293	37	172	4·6487	56	275	4·9107	53	273	5·1509
39	36	182	5·0556	15	58	3·8667	42	235	5·5952	30	180	6·0000
40 and over	53	277	5·2264	67	396	5·9104	116	711	6·1293	73	438	6·0000
36 and over	235	1,051	4·4723	204	993	4·8676	339	1,831	5·4012	268	1,465	5·4664
All Ages ..	3,196	8,006	2·5050	2,697	6,903	2·5595	3,711	10,030	2·7028	3,281	9,199	2·8037

mother, and we have been able to construct a Table showing the A-B-O mother-child combinations for 16,179 single births which occurred to women of English and non-English name during the period 1944–48 and 1952–53 (Table VI). The expected number of children for each combination was calculated by assuming that the mothers were mated at random with a sample of fathers having the same

TABLE VI

MOTHER-CHILD COMBINATIONS IN MELBOURNE SAMPLE 1944–48 + 1952–53. (SINGLE BIRTHS ONLY)

Blood Group of Children			Blood Group of Mothers				
			O	A	B	AB	All Groups
No. of Children	O	(observed)	5,334	1,879	539		7,752
		(estimated)	(5,172·32)	(1,862·30)	(529·77)		(7,564·39)
	A	(observed)	1,754	4,124	218	273	6,369
		(estimated)	(1,862·30)	(4,115·30)	(190·75)	(259·42)	(6,427·77)
	B	(observed)	497	218	681	226	1,622
		(estimated)	(529·77)	(190·75)	(698·11)	(210·28)	(1,628·92)
	AB	(observed)		185	167	84	436
		(estimated		(259·42)	(210·28)	(88·22)	(557·92)
All Groups		(observed)	7,585	6,406	1,605	583	16,179
		(estimated)	(7,564·39)	(6,427·77)	(1,628·91)	(557·92)	(16,178·99)

blood-group distribution as the mothers. In the absence of information on the real blood-group distribution of the fathers this assumption seems to be the most reasonable one to adopt.

There is a theoretical objection to this pooling of the results for the English and non-English name samples. The expectations calculated by using the gene frequencies from the total sample will be different from the expectations derived from the gene frequencies of the English and non-English name groups treated as separate isolates. We have carried out the calculations for the 1952 and 1953 sample by using both the gene frequencies calculated separately for the women of English and non-English name and gene frequencies based on the pooled sample. The difference between the expected numbers obtained by these two methods is approximately 0·1 per cent. We consider, therefore, that the errors introduced by using gene frequencies based on the total sample for 1944–48 and 1952–53 will be rather less than 0·1 per cent., if the other assumption on the gene frequency of the fathers is valid. The gene frequencies have been calculated by the method of maximum likelihood (Stevens, 1938), and the values finally used were $p = 0{\cdot}246{,}193$, $q = 0{\cdot}070{,}035$, and $r = 0{\cdot}683{,}772$.

A comparison of the observed and expected values reveals discrepancies of the kind noted in our earlier paper (Bryce and others, 1950). The χ values for each compartment of Table VI are given in Table VII. From this it will be seen that there are significant deficiencies of group A children to group O mothers, and of group AB children to both group A and B mothers. There are also significant excesses of group O children to group O mothers, of group B children to group A mothers, and of group A children to group B mothers. The direct evaluation of the mother-infant blood-group relationship of all 16,179 cases examined also reveals a highly significant difference ($\chi^2 = 23{\cdot}22$; $P < 0{\cdot}001$).

TABLE VII

χ^2 FOR DIFFERENCES BETWEEN OBSERVED AND CALCULATED VALUES IN TABLE VI

Blood Group of Children	Blood Group of Mothers				
	O	A	B	AB	All Groups
O	+2·248	+0·387	+0·401	·	+2·157
A	−2·510	+0·136	+1·973	+0·843	−0·733
B	−1·424	+1·973	−0·648	+1·084	−0·171
AB		−4·621	−2·985	−0·450	−5·162

If the discrepancies noted above are due to the selective action of immune antibodies reacting with foetal tissues we might expect the distribution of mother-child combinations to be different for first-born, second-born, third-born children, etc. This can be investigated for single births in the Melbourne 1952–53 sample. If the number of group A and B children to group O mothers is compared with the group O children to group A and B mothers respectively (Table VIII), it will be seen that there is no deficiency in the former case for first-born children. There is, however, a marked deficiency for second- and third-born group A and B children to group O mothers when compared with second- and third-born group O children to group A and B mothers, though the difference disappears again for the fourth and higher-born children. The expected number of each birth rank has been calculated using the gene frequencies based on the total mother sample. A comparison of the observed and expected values for each birth rank in each mother-child combination confirms the conclusions reached above which were based on direct comparisons within the body of the Table.

TABLE VIII

MOTHER-CHILD COMBINATIONS BY BIRTH RANK IN MELBOURNE SAMPLE 1952–53

(Single Births only)

Blood Group of Children	Birth Rank	Blood Group of Mothers				
		O	A	B	AB	All Groups
O	1 ..	881	287	81		1,249
	2 ..	754	272	90		1,116
	3 ..	475	187	52		714
	4 ..	269	92	17		378
	5 and over	278	106	23		407
A	1 ..	287	649	40	53	1,029
	2 ..	236	615	27	32	910
	3 ..	146	389	12	23	570
	4 ..	92	196	11	17	316
	5 and over	93	217	11	16	337
B	1 ..	79	32	109	34	254
	2 ..	78	33	112	48	271
	3 ..	33	17	65	23	138
	4 ..	15	11	32	14	72
	5 and over	26	11	38	11	86
AB	1 ..		28	22	19	69
	2 ..		34	28	7	69
	3 ..		12	13	7	32
	4 ..		5	11	2	18
	5 and over		10	9	1	20
All Groups	1 ..	1,247	996	252	106	2,601
	2 ..	1,068	954	257	87	2,366
	3 ..	654	605	142	53	1,454
	4 ..	376	304	71	33	784
	5 and over	397	344	81	28	850
All Ranks	.. ..	3,742	3,203	803	307	8,055

These results would suggest that the observed deficiency of group A and B children to group O mothers might well be due to the operation of an immune response mechanism. On the other hand it is interesting to note that the marked deficiency of group AB infants to both group A mothers and

group B mothers is present for first-born children as well as for those of higher rank. Similarly the observed excess of group B children to group A mothers and group A children to group B mothers shows no relationship to birth rank. A larger sample would need to be analysed for any significance to be attached to the discrepancies noted in these latter cases.

Discussion

The present study of two large samples of mothers from Australian maternity hospitals is of interest for the current discussion of selective action within the ABO blood-group system. This problem has been reviewed recently by Neel (1954) and it is clear that even though nearly 30 years have elapsed since Hirszfeld and Zborowski (1925) first noted the deficiency of group A children in families where the mother is group O and the father group A there has still been no satisfactory assessment of all the evidence now available.

Levine (1943) collected evidence which supported Hirszfeld's original view that matings A ♂ × O ♀ produced fewer offspring than reciprocal matings O ♂ and A ♀. Waterhouse and Hogben (1947) in a more detailed study of the same problem arrived at similar conclusions for their A × O matings, though the B × O matings showed a discrepancy opposite to that which would be expected on the basis of selection in incompatible mating groups.

Waterhouse and Hogben's work has been criticized recently by Bennett and Brandt (1954). This criticism rests in part on the heterogeneity of families segregating for group A and O children in the twelve samples included in their survey. Waterhouse and Hogben drew on family studies of ABO blood-groups carried out in a number of different countries. Matsunaga (1953) has now made a similar study based solely on Japanese material and finds a significant deficiency of children in matings A ♂ × O ♀ and B ♂ × O ♀. In a further study of two mining communities in Hokkaido, Matsunaga and Itoh (1954) have demonstrated a highly significant reduction in the number of living children for women in A-B-O incompatible mating groups compared with those in compatible mating groups.

A different approach was made to the problem by Boorman (1950) and by Bryce and others (1950). If group A or B children are being selectively eliminated by group O mothers, the mother-child combinations for large unselected samples of mothers having babies should reveal deviations from expectation. In both these studies there was no significant deficiency of group A or B children born to group O mothers, though in the much larger Australian sample studied by Bryce and others (1950) a marked deficiency was found in group A children to O mothers. These authors draw attention in their work, however, to much bigger discrepancies, which are present also in Boorman's study, principally the deficiency of group AB children to A and B mothers, and the excess over expectation of group B children to group A mothers and group A children to group B mothers. These two latter discrepancies are difficult to reconcile with the concept of foetal loss through selection in incompatible matings, since both A mother-B child and B mother-A child are incompatible. A somewhat similar study by Johnstone (1954) of an English maternity hospital sample included the blood groups of the fathers as well as of the mothers and children He found no deficiency of group A children in matings A ♂ × O ♀ and points out that if the expectations are distributed in the usual way there is in fact a significant deficiency of group O children in matings O ♂ × A ♀. This discrepancy, too, is difficult to reconcile with incompatible selection as ordinarily defined, nor are we yet aware of any clinical or serological evidence which could account for the magnitude of the selective effect stated for the loss of group O children to group A mothers.

Data based on maternity hospital samples of the kind published by Boorman (1950) and Johnstone (1954) must be interpreted with caution when use is made of them for comparison with studies such as those of Waterhouse and Hogben, and Matsunaga. In these latter investigations the material was collected in the main for studies of inheritance of particular genes, so that the proportion of one-child families was low. In both Boorman's and Johnstone's samples, however, the mean number of pregnancies per woman was less than two, approximately 50 per cent. of the mothers being primiparae. If selective action within the ABO blood groups is in any way comparable to that in the Rh system, very much larger samples than those presented by Boorman and Johnstone would be required to manifest the effects they were looking for if the majority of the women in the sample are experiencing only their first or second pregnancy.

Indeed such information relevant to the question of the influence of incompatibility on pregnancy experience as can be extracted from their published data suggests that selective action is occurring in higher birth-ranks. In Boorman's data the mothers who are classed as incompatible for the A antigen suffer a marked deficiency in their pregnancy experience above the age of 20 compared with compatible mothers, the difference increasing with age. At age 40–49 the figures are 2·91 and 3·86.

Similarly an examination of Table VIa of Johnstone's paper reveals a significant deficiency of mothers experiencing their fourth or higher pregnancy in the mating group A ♂ × O ♀ compared with O ♂ × A ♀ (for the whole table $\chi^2 = 10{\cdot}392$; 4.*d.f.*; $0{\cdot}05 > P > 0{\cdot}02$).

Our own studies of two Australian maternity hospital samples emphasize the necessity for caution in interpreting samples of this kind. Drawn from two separate populations, the Perth and Melbourne samples are significantly different from one another in age structure and overall pregnancy experience per woman. Using a simple name analysis, both samples can be broken up into an English and non-English name group, there being a highly significant difference in blood-group frequency between the English and non-English name groups for both places. It is possible that the use of more refined techniques could split each of these samples into a still larger number of groups of more homogeneous composition.

A comparison of the English name groups in each sample brings out the following points. Group A women in both samples have experienced slightly more pregnancies than have group O women. The difference is significant for the Perth sample but not so for Melbourne. A more detailed study of the difference in pregnancy experience by each year of age for group O and A women suggests, however, that the tendency for group A women to experience an increasingly large number of pregnancies with increasing age as compared with group O women is true in Melbourne as well as in Perth. That the differences are much smaller in the Melbourne sample is undoubtedly due to the highly significant difference in pregnancy experience of the women in the two samples.

A comparison of the expected and observed number of children in various mother-child combinations for ABO blood groups reveals a number of significant discrepancies. The highly significant deficiencies of group A children to group O mothers and of group AB children to group A and B mothers supports the hypothesis that mother-child incompatibility is eliminating a proportion of the incompatible children. This simple explanation, however, cannot account for the observed excess of group B children to group A mothers and of group A children to group B mothers. These latter discrepancies still await a satisfactory explanation.

A study of mother-child combinations by birth rank for the Melbourne sample shows no deficiency of group A or B children born to group O mothers in the first birth rank, but a marked deficiency in the second, and an even greater deficiency in the third.

This study lends support to the concept that a proportion of women of blood group O progressively suffer a reduction in fertility due to the operation of selection in incompatible pregnancies. Many of the other possibilities related to the general problem of blood group polymorphism in man must await the accumulation of still larger samples before answers approaching the decisive can be given to the questions raised.

Summary

(1) Two Australian maternity hospital samples have been analysed to throw light on the problem of incompatibility between mother and child within the ABO blood-group system. The first sample comprised mothers entering the Queen Victoria Hospital, Melbourne, during the years 1944–48 and 1952–53. The other sample comprised mothers entering the King Edward VII Maternity Hospital, Perth, during the years 1948–53.

(2) The Melbourne and Perth samples revealed highly significant differences in blood-group distribution between women of English and non-English name, but there were no significant differences in blood-group distribution between the Melbourne and Perth samples for women of English name, or for women of non-English name compared separately. Melbourne and Perth did differ significantly, however, in the age composition and in the overall pregnancy experience of all women in the samples.

(3) In both Melbourne and Perth group A women had a higher average number of pregnancies than group O women. The difference was significant for Perth but not for Melbourne. The curve fitted to the difference in mean number of pregnancies between the two groups of women for each year of age from 16–40 showed a significant linear increase in the difference group A — group O for Perth. The same trend was present for the Melbourne sample below age 35, but the greater variability in this sample above that age reduced the significance of the trend over the entire age range studied. The discrepancy between the two samples is due probably to the smaller average number of pregnancies of women in the Melbourne sample.

(4) A comparison of the calculated and observed number of children in different mother-child blood-group combinations for 16,179 single births in Melbourne reveals a significant deficiency of group A children to group O mothers and group AB children to group A and B mothers, and a significant excess

of group O children to group O mothers, of group A children to group B mothers, and group B children to group A mothers.

(5) A breakdown of mother-child blood-group combinations by birth rank reveals that the deficiency of group A and B children to group O mothers is absent for first-born children, present for second-born children, and greatest for third-born children.

(6) These results are discussed in relation to other work of a similar kind, and it is suggested that the results presented support the hypothesis that incompatibility between mother and child in the ABO blood-group system results in selective loss of a proportion of incompatible children.

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